REPORT DOCUMENTATION PAGE

READ INSTRUCTIONS BEFORE COMPLETING FORM

1. REPORT NUMBER: NADC-84101-60	2. GOVT ACCESSION NO.
3. RECIPIENT'S CATALOG NUMBER	
4. TITLE (and Subtitle): Assessment of Human Visual Performance with a Swept Evoked Potential Technique	5. TYPE OF REPORT & PERIOD COVERED: Final Report
6. PERFORMING ORG. REPORT NUMBER	
7. AUTHOR(s): Jeremiah I. Nelson, Ph.D.	8. CONTRACT OR GRANT NUMBER(s): N62269-82-C-0247
9. PERFORMING ORGANIZATION NAME AND ADDRESS: Dept. Ophthalmology PHL 811 NYU Medical Center 550 First Avenue New York, NY 10016	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
11. CONTROLLING OFFICE NAME AND ADDRESS: Naval Air Systems Command Dept. of the Navy Washington, DC	12. REPORT DATE: July 1984 13. NUMBER OF PAGES: 57
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office): Naval Air Development Center Aircraft & Crew Systems Technology Directorate Warminster, PA 18974	15. SECURITY CLASS. (of this report): UNCLASSIFIED 15a. DECLASSIFICATION/DOWNGRADING SCHEDULE

16. DISTRIBUTION STATEMENT (of this Report)

Approved for public release; Distribution Unlimited

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Orientation contrast effects
Stimulus Orientation
Visual Perception

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

A Final Report is presented for a project in visual assessment with the visual evoked response (VER). Methods have been perfected for telling how well a person can see by direct measurement of his brain's response. Visual performance is measured in terms of contrast sensitivity and the acuity limit. The acuity limit is similar to the resolution limit measured by familiar Snellen eye charts. "Contrast" is familiar from the contrast control of TV sets; fading out contrast until very faint light-dark differences are reached

provides a means of testing sensitivity to large patterns (a ship at sea in fog), where resolution of fine detail is not the problem.

In this work, an observer with scalp electrodes over the visual areas of his brain views striped patterns on a TV monitor. Modern signal retrieval techniques are used to enhance weak visual responses in the noisy signals coming from the scalp electrodes.

The specific aims of the contract have all been realized, providing
1) validation of the technique,
2) generation of evidence that contributions from the newly discovered X and Y visual pathways can be separated in the gross scalp potential with this new technique, and
3) identification of noise contamination is some observed responses.

These research areas are considered in turn.

In addition, the rapidity with which striped patterns of many orientations may be tested has made it possible to discover that, in multiple sclerosis cases, visual performance damage can occur in only one orientation range. This implies an unsuspected specificity for a disease thought to attack randomly, as well as an unsuspected involvement in cortical grey matter (where orientation detection normally occurs) for a disease commonly thought to involve principally white matter (for example, the spinal cord and other nerves).

This work serves to transform the evoked potential from a complex waveform of obscure origin to a tool for visual research and testing.

REPORT NO. NADC-84101-60

ASSESSMENT OF HUMAN VISUAL PERFORMANCE WITH A SWEPT EVOKED POTENTIAL TECHNIQUE

Jeremiah I. Nelson, Ph.D..
Dept. Ophthalmology PHL 811
NYU MEDICAL CENTER
550 First Avenue
New York, NY 10016

JULY 1984

FINAL REPORT
CONTRACT NO. N62269-82-C-0247

APPROVED FOR PUBLIC RELEASE; DISTRIBUTION UNLIMITED

Prepared for
NAVAL AIR SYSTEMS COMMAND
Department of the Navy
Washington, D.C. 20361

NOTICES

REPORT NUMBERING SYSTEM – The numbering of technical project reports issued by the Naval Air Development Center is arranged for specific identification purposes. Each number consists of the Center acronym, the calendar year in which the number was assigned, the sequence number of the report within the specific calendar year, and the official 2-digit correspondence code of the Command Office or the Functional Directorate responsible for the report. For example: Report No. NADC-78015-20 indicates the fifteenth Center report for the year 1978, and prepared by the Systems Directorate. The numerical codes are as follows:

CODE	OFFICE OR DIRECTORATE
00	Commander, Naval Air Development Center
01	Technical Director, Naval Air Development Center
02	Comptroller
10	Directorate Command Projects
20	Systems Directorate
30	Sensors & Avionics Technology Directorate
40	Communication & Navigation Technology Directorate
50	Software Computer Directorate
60	Aircraft & Crew Systems Technology Directorate
70	Planning Assessment Resources
80	Engineering Support Group

PRODUCT ENDORSEMENT – The discussion or instructions concerning commercial products herein do not constitute an endorsement by the Government nor do they convey or imply the license or right to use such products.

TABLE OF CONTENTS

	Page
List of Figures	ii
List of Tables	iii
Title Page	1
Contents	2
Abstract	4
Development of the Technique	5
Validation of the Technique	10
The Separation of X- and Y- Dominated Visual Evoked Responses	20
The Intrusion of EEG Noise Upon Visual Responses and Response Baselines	33
Recent Findings: Orientation and Spacial Frequency Selective Losses in Multiple Sclerosis	39
Conclusion	50
References	51

LIST OF FIGURES

Figure		Page
1.	Contrast sensitivity determination	6
2.	Contrast sensitivity determination	7
3.	Acuity measurement	8
4.	Acuity measurement	9
5.	Contrast sensitivity function	15
6.	Contrast sensitivity functions	16
7.	Contrast sensitivity functions	17
8.	Oblique effect in contrast threshold for four observers	22
9.	Oblique effect abolished	23
10.	Oblique effect abolished	24
11.	Oblique effect in acuity for four observers	26
12.	Oblique effect diminution	27
13.	Discrete potential generations (?)	30
14.	Strobe stimulation responses	32
15.	Random phase EEG	34
16.	Phase sensitive detection	35
17.	Frequency selectivity	36
18.	Zero response level	38
19a.	Contrast thresholds	42
19b.	Contrast thresholds	43
20.	Contrast thresholds	45
21.	Contrast thresholds	46
22.	Contrast thresholds	48

LIST OF TABLES

Table — Page

1. VER - and Psychophysically - defined Contract Sensitivity Thresholds ---------- 14

2. The Oblique Effect in Acuity and Contrast Sensitivity ---------- 25

ASSESSMENT OF HUMAN VISUAL PERFORMANCE with a SWEPT EVOKED POTENTIAL TECHNIQUE

Final Report for Contract N62269-82-C-0247
1 April 1982 - 31 March 1983
Naval Air Systems Command
Warminster, PA 18974
attn: Gloria Chisum; Leon Hrebien

Jeremiah I. Nelson, Ph.D., Principal Investigator
Department of Ophthalmology PHL811
New York University Medical Center
550 First Avenue
New York, NY 10016 212/340-6890

CONTENTS

4 **ABSTRACT**

I. DEVELOPMENT OF THE TECHNIQUE

5 Computer averaging has shortcomings
5 Illustration of the paradigm.

PART II. VALIDATION OF THE TECHNIQUE

10 Contrast sensitivity
11 Methods
11 Subjects.
12 Stimuli.
12 Responses.
12 Experimental procedure.
12 Threshold estimation.
13 Psychophysics.
13 Results
14 **Table 1**
18 Discussion

PART III. THE SEPARATION OF X- AND Y-DOMINATED VISUAL EVOKED RESPONSES

20 Background on X and Y visual subsystems
20 The new visual duplicity.
21 Methodological details
21 Subjects, optics.
21 Response.
21 Threshold estimation.
21 Results
21 Swept contrast.
24 Swept spatial frequency: acuity limit.
25 **Table 2**
27 Discussion.
28 Neurophysiological substrate for the oblique effect.
29 Are the cells which bring us the oblique effect IN the X stream?
29 Other evidence for XY separation at threshold.
29 Other studies of the oblique effect's spatiotemporal limits.
30 A Y-generated peak at 43 reversals/sec

PART IV. THE INTRUSION OF EEG NOISE UPON VISUAL RESPONSES and RESPONSE BASELINES

33 EEG Interference
33 EEG phase is random.
34 Rise after threshold.
37 A frequency-selective instrument sees coherent noise.
37 The baseline: extrapolation to what?

PART V.

RECENT FINDINGS: ORIENTATION AND SPATIAL FREQUENCY SELECTIVE LOSSES in MULTIPLE SCLEROSIS

39 Introduction
40 Methods
40 Stimuli.
40 Responses.
41 Experimental paradigm.
41 Patients.
42 Results
47 Discussion
47 Cortical involvement.
49 Selective loss and functional architecture.
49 Other possibilities.
50 Swept technique advantages

50 **CONCLUSION**

51 **REFERENCES**

ABSTRACT

A Final Report is presented for a project in visual assessment with the visual evoked response (VER). Methods have been perfected for telling how well a person can see by direct measurement of his brain's response. Visual performance is measured in terms of contrast sensitivity and the acuity limit. The acuity limit is similar to the resolution limit measured by familiar Snellen eye charts. "Contrast" is familiar from the contrast control of TV sets; fading out contrast until very faint light-dark differences are reached provides a means of testing sensitivity to large patterns (a ship at sea in fog), where resolution of fine detail is not the problem.

In this work, an observer with scalp electrodes over the visual areas of his brain views striped patterns on a TV monitor. Modern signal retrieval techniques are used to enhance weak visual responses in the noisy signals coming from the scalp electrodes.

The specific aims of the contract have all been realized, providing
1) validation of the technique,
2) generation of evidence that contributions from the newly discovered X and Y visual pathways can be separated in the gross scalp potential with this new technique, and
3) identification of noise contamination in some observed responses.

These research areas are considered in turn.

In addition, the rapidity with which striped patterns of many orientations may be tested has made it possible to discover that, in multiple sclerosis cases, visual performance damage can occur in only one orientation range. This implies an unsuspected specificity for a disease thought to attack randomly, as well as an unsuspected involvement in cortical grey matter (where orientation detection normally occurs) for a disease commonly thought to involve principally white matter (for example, the spinal cord and other nerves).

This work serves to transform the evoked potential from a complex waveform of obscure origin to a tool for visual research and testing.

PART I. DEVELOPMENT OF THE TECHNIQUE

Computer averaging has shortcomings

The central problem in this project, as with most forms of electrophysiological research with human subjects, is retrieval of a weak signal. The computer of average transients or "averager" is the most common instrument for signal retrieval. Computer averaging of visual evoked responses (VERs), whether these are so called "transient" or "steady state" responses, retrieves the actual waveshape of discrete evoked responses. This signal-to-noise enhancement process is based on building up the response through superimposition. Obviously it must be assumed that the many weak responses being summed together are identical. This assumption works well in practice, although in fact there are amplitude and waveshape variations (Childers, Doyle, Brinck and Perry, 1972; general critique in Aunon, McGillem & Childers, 1981) for which sophisticated signal processing remedies are available (Senmoto and Childers, 1972). Particularly for late components, one should be circumspect in viewing the output of an averager as a picture of the true and only possible evoked potential waveform.

Computer averaging easily reveals a response to a sudden stimulus (e.g., flash of light) after the stimulus has been repeated 50 to 100 times. The evoked potential's waveshape and latency provide an objective assessment of neural pathway conduction in the visual system. However, aspects of the electrical waveform data which can be related to visual performance or visual complaints in a clinical setting are limited. Only with great difficulty can sufficient data be won for making inferences about threshold performance (Campbell and Maffei, 1970). Such studies entail obtaining a response, changing the stimulus (e.g., resetting the contrast), obtaining another response, and so forth, which can take hours per subject. A plot of decreasing response amplitude vs. decreasing stimulus strength may then be derived and extrapolated to that stimulus at which evoked response would have been zero. This point is an electrophysiologically derived estimate of visual threshold.

Illustration of the paradigm. Following the pioneering lead of Regan (1973), we have speeded the extrapolation-to-zero method to the point where thresholds may be inferred in 20 seconds. The development of the technique may be illustrated in two steps. First, one could electronically change the desired stimulus parameter in time. In Fig. 1, contrast increases slowly from 1 to 25% over a period of 2 seconds while the pattern reverses seven times per second. The tedium of resetting the stimulus is removed, and the change in response amplitude serves to define a threshold. Here, the oscillatory response is seen to rise from zero at a contrast of 2.9%. However, the presentation must be repeated hundreds of times over a period of 8 minutes before the desired response is obtained.

With stimulus presentation automated, attention turns to the response. Instrumentation is available which can retrieve response amplitude information for a selected frequency (i.e., retrieve a point on the power spectrum). Retrieval is performed in real time, obviating the necessity of computer averaging. Output is based on total wave information rather than merely upon the peaks as in Fig. 1, and takes the form of a slowly varying DC level indicative of the strength of the selected sine wave. Since we know the steady state evoked potential is sinusoidal in form and desire only a

measure of amplitude, this method is well suited to our purposes; little information is discarded.

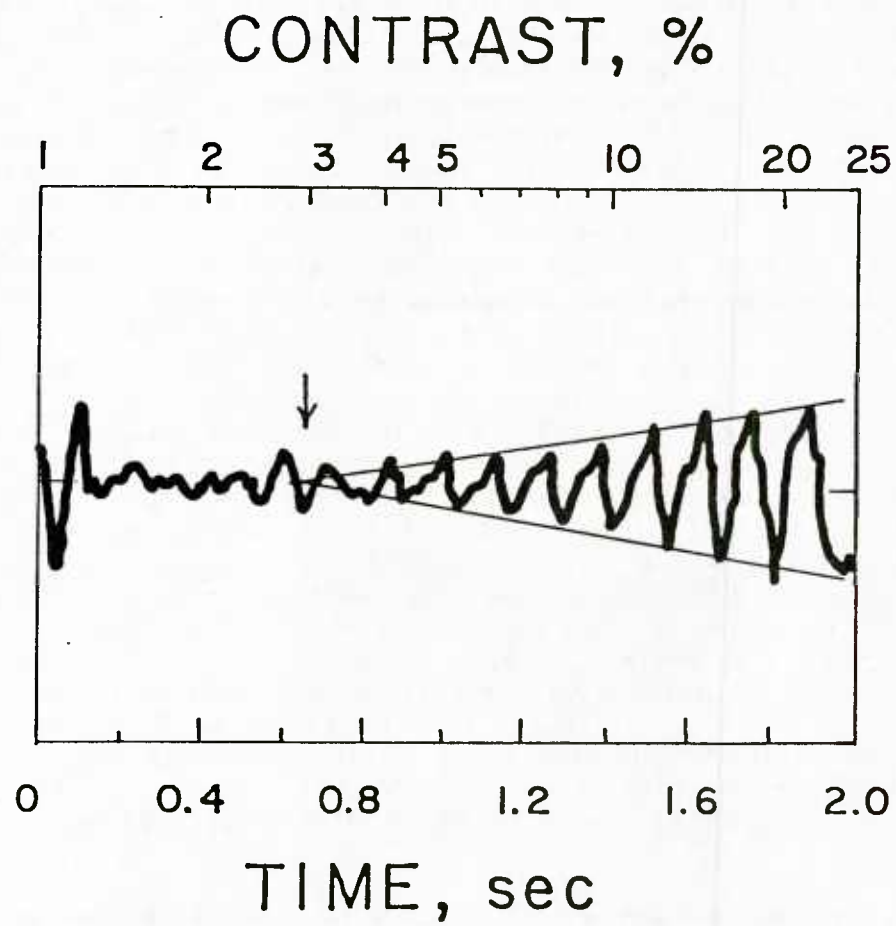


Fig. 1. Contrast sensitivity determination. Conventional computer averaging reveals the brain's evoked response waveform during visual stimulation which is swept upward in contrast. This sweep is a logarithmic increase of contrast from 1 to 25%; the contrast increase causes the response to grow from left to right. The zero response point provides an objective estimate of contrast threshold (2.9%, **arrow**). This is what the contrast would have been for the smallest possible brain response. Repeating this measurement with other spatial frequencies would define a contrast sensitivity function (modulation transfer function; see Section II). Unfortunately, the computer averaging time for the single response illustrated was 8 minutes plus rest periods. Therefore we have replaced computer averaging with lock-in retrieval (next Figure). Two cycles/deg sine grating, 7 reversals/sec.

The instrumentation referred to is the lock-in amplifier. Fig. 2 illustrates the results obtained with lock-in techniques. The output is a slowly changing voltage level which traces the amplitude envelope of the underlying steady state wave form. The lock-in achieves signal retrieval through frequency selectivity. Frequency selectivity is achieved with synchronous demodulation methods, not with conventional tuned circuits (filters). Equivalent noise bandwidths of 0.04 Hz are routinely attained, without the ringing associated with filters.

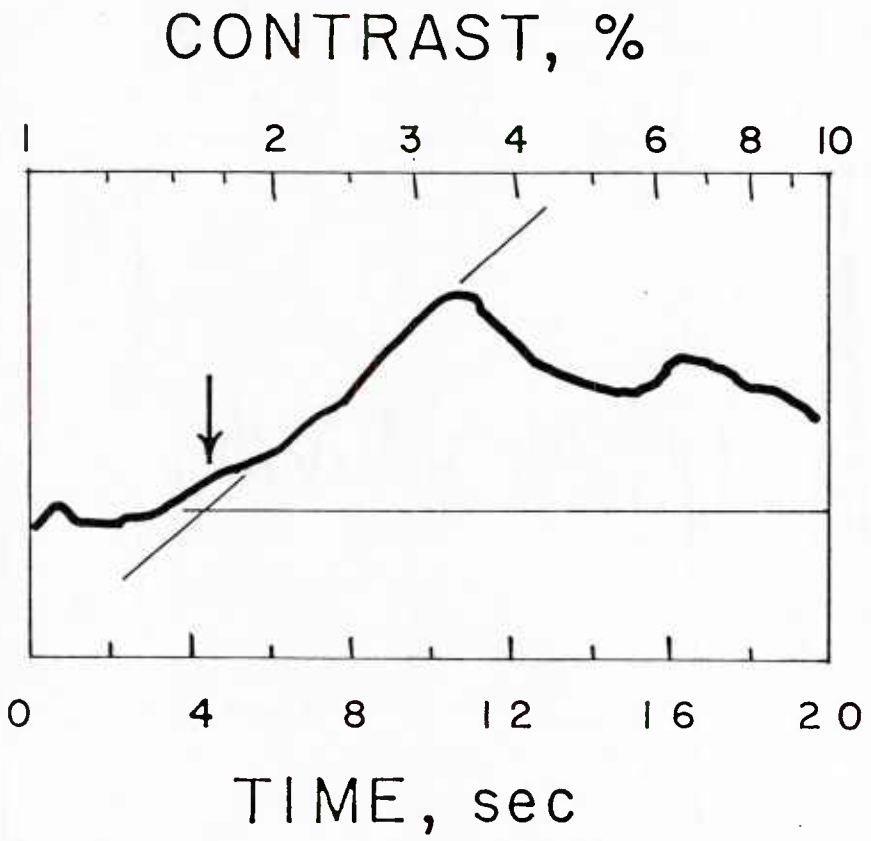


Fig. 2. Contrast sensitivity determination. Signal retrieval with lock-in techniques provides a slowly varying DC level proportional to the overall response amplitude envelope illustrated in the previous Figure. Information concerning the shape of the response within the envelope is lost, but speed is gained. Contrast threshold (1.7%, **arrow**) was determined in 20 seconds. Two cycles/degree sine grating, 12.8 reversals/sec.

Turning from contrast to spatial frequency sweeps, we note that evoked amplitude varies logarithmically with contrast (Campbell & Maffei, 1970.) Consequently, increasing contrast logarithmically in time as illustrated above linearized the observed stimulus-response function, greatly facilitating extrapolation to zero amplitude (inferred threshold). For spatial frequencies near the acuity limit, spatial frequency increases are

equivalent to contrast reductions, ultimately reaching the point where the pattern washes out entirely and can no longer be resolved. This effective contrast decrease is itself logarithmic with spatial frequency, so that a spatial frequency sweep which is linear with time will produce a response which falls linearly to the acuity limit. Such a decreasing response waveform, retrieved with lengthy computer averaging, is shown in Fig. 3. Lock-in techniques retrieve the amplitude envelope of this response without the waveform information, as shown in Fig. 4.

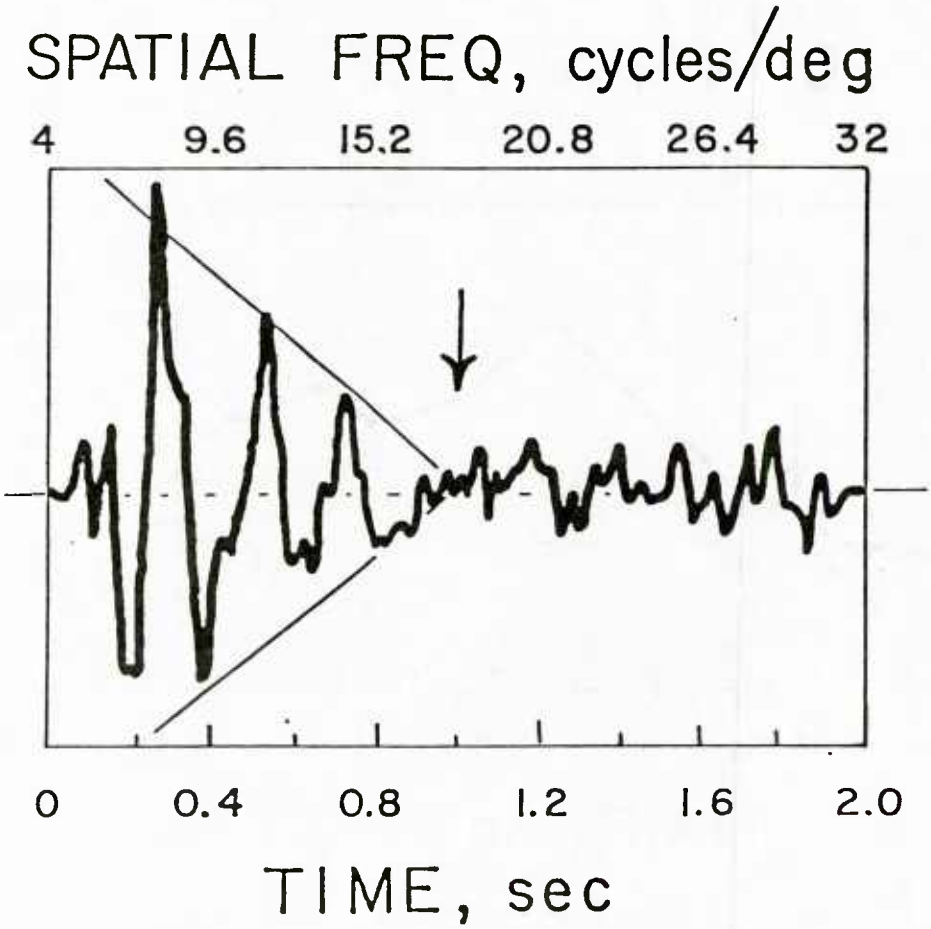


Fig. 3. Acuity measurement. The visual system's cortical evoked response decreases as spatial frequency approaches the acuity limit. The subject's acuity limit may be inferred from the spatial frequency on the display at the instant the visual evoked response amplitude reaches zero; here, 18 cycles/deg (**arrow**). Four to 32 cycles/deg sine wave grating, 40% contrast, 5 Hz reversal rate, retrieval of response with lengthy computer averaging.

This methodology for contrast and spatial frequency response limit determinations was the basis of the studies reported here. I term the technique the VSCAN for Visual Scan.

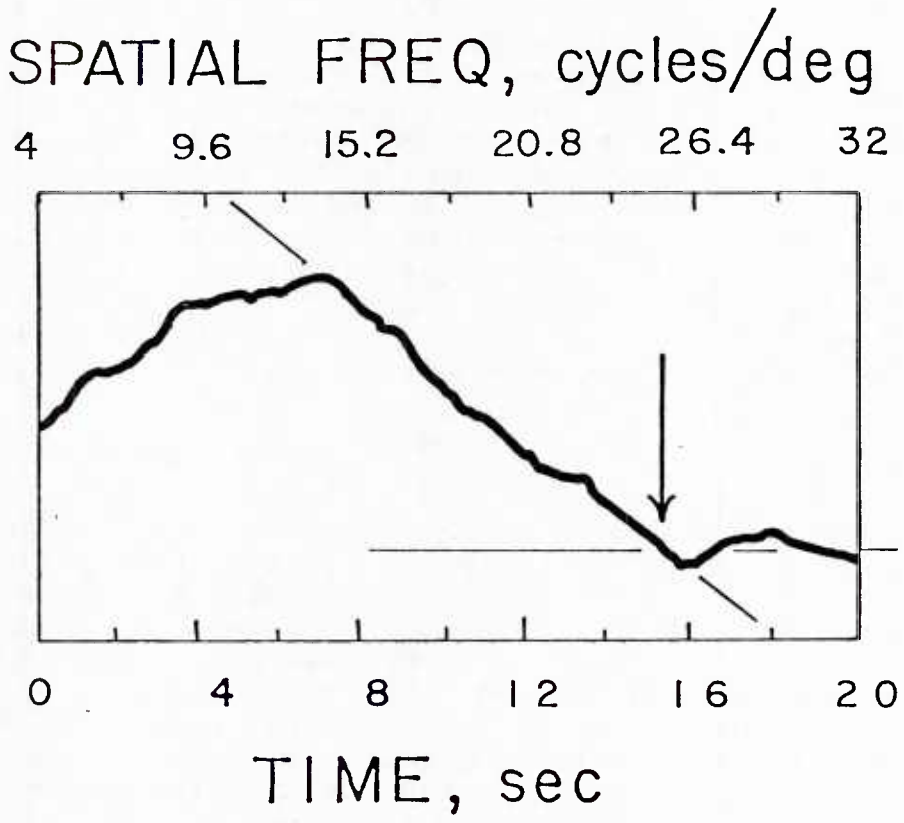


Fig. 4. Acuity measurement. Visual signal retrieval from noisy scalp potentials is performed with lock-in techniques for the same stimulation conditions as previous Figure, except that reversal rate is 13 Hz. Apparent threshold (**arrow**) of 25.3 cycles/deg is superior to the 18 cycles/deg in the previous figure. This may occur because fatigue and adaptation are minimized by the speed of the real time retrieval method.

PART II. VALIDATION OF THE TECHNIQUE

The swept technique is rapid, objective and easily applied to subjects under a wide variety of circumstances. However, with trained observers under laboratory conditions, psychophysical techniques offer the greatest accuracy. Therefore, we wished to use psychophysical methods to evaluate the validity of the swept evoked potential. We compared contrast thresholds estimated directly from scalp potentials with thresholds measured by a conventional psychophysical technique using the same subjects and the same stimulus conditions. The particular psychophysical technique was the method of adjustment, in which the observer increased contrast until a pattern became visible (ascending limit), then decreased contrast until the stimulus field appeared homogeneous. The average of equal numbers of well-replicated ascending and descending limits is taken as the contrast threshold. The swept VER was compared to those thresholds with regard to both sensitivity and reliability.

Contrast sensitivity

In general, contrast sensitivity is assessed by reducing the difference between the lightest and darkest parts of a pattern until it becomes impossible either to detect or to identify the pattern. Such patterns are most conveniently generated on cathode ray tube (**CRT**) screens. Because the imposition of some pattern of light and dark areas is the imposition of a modulation on an otherwise uniform grey field, contrast sensitivity is seen to be a form of modulation threshold. An especially powerful pattern of modulation to use is a sinusoidal change in luminance as one proceeds across the screen. If one performs a dead repeat of this modulation for every scan line across the screen, a pattern of blurry stripes results. This is a sinusoidal grating.

A sinusoidal grating is to vision what a sine wave oscillator's signal is to electrical engineering: the response of any amplifier, filter or other circuitry may be defined in terms of how much signal it passes for sine wave test signals of all frequencies across the range of interest. Having made this measurement for pure sine waves, one may specify the circuit's response to any arbitrary waveform, since a waveform of any complexity may be analyzed into a series of sinusoidal components. For the visual system, the sensitivity to a broad range of sinusoidal spatial frequencies should enable us to predict the visual system's fidelity in responding to any visual scene one might encounter in a lifetime. The only wrinkle is that an amplifier works on a single signal, while visual targets are spread out across space. To deal with the two-dimensional nature of spatial vision, the contrast sensitivity function (**CSF**) should be repeated for at least two sets of gratings with stripes at right angles to each other. By appropriately combining results for two orientations at right angles to each other, responses to stimuli at any intermediate angle may be predicted. In summary, the contrast sensitivity function brings to vision the power and generality of Fourier theory. How can we bring contrast sensitivity testing to routine visual assessment?

The contrast sensitivity function (**CSF**) is a form of modulation transfer function which can be used to predict visual detection performance for any real-life target. The utility of the CSF has long been appreciated (Campbell & Green, 1965.) Estimates of visual contrast threshold performance across the entire spatio-temporal domain add information not provided by Snellen acuity values, as these deal only with high spatial frequency at high contrast. The CSF sheds light upon visual changes related to age (Arundale, 1978; Sekuler, Hutman & Owsley, 1980), refractive error (Enoch, Shinichi & Namba, 1979), and various ophthalmological and neurological diseases (Arden, 1978; Regan, Silver & Murray, 1977). We now have a means to obtain the desired contrast sensitivity information electrophysiologically; here, the method is used to obtain entire CSFs for four subjects, and to compare these CSFs to values obtained psychophysically under identical conditions in our laboratory, and under more varied psychophysical conditions as published in the literature.

The most common method of measuring human contrast thresholds has been psychophysical (Robson, 1966; Kelly, 1977). Some attempts have been made to automate psychophysical procedures using von Bekesy tracking methods with a monitor made to automatically increase and decrease stimulus contrast (Sekuler & Tynan, 1977; Ginsburg & Cannon, 1983), or by using plates with one spatial frequency modulated in contrast across the page (Arden, 1978; an occluding piece of cardboard is slid across the page until the observer reports detection of the striped pattern). However, in all these attempts, some accuracy has been sacrificed and excellent subject cooperation is always required.

Electrophysiological techniques offer the possibility of assessing the CSF directly, using the visual system's response. However, only a few researchers have attempted contrast threshold measurements (Campbell & Kulikowski, 1971; Campbell & Kulikowski, 1972; Campbell & Maffei, 1970; Kulikowski, 1978), mainly because conventional computer averaged evoked potentials require lengthy recording periods to retrieve the desired responses, particularly for feeble stimuli near threshold. Further, the averaged potentials can be contaminated by fatigue and adaptation. In sum, CSFs estimated from evoked potentials have been difficult for laboratory researchers and unfeasible for clinical populations. An approach which utilizes real-time retrieval of visual responses to continuously changing stimuli (e.g., contrast levels sweeping in time) minimizes some of these difficulties. Such methods have been pioneered in the study of evoked potential responses to spatial frequency (Regan, 1973; Tyler, Apkarian, Levi & Nakayama, 1979) and color (Regan, 1975). Using an extension of these methods, we have been able to measure contrast and acuity thresholds (Nelson, Kupersmith, Seiple & Carr, 1982). Here, complete CSFs have been determined for a number of temporal frequencies.

Methods

Subjects. Three males and one female between the ages of 31 and 39 served as subjects. All had normal vision correctable to 6/6 and no history of neurological or ophthalmological disease. They were experienced psychophysical observers and acquainted with the purpose of the experiment.

Stimuli. Sine wave gratings generated by a pattern generator were displayed on a Conrac Model QQA 14N/A video monitor at a mean luminance of 50 cd/m^2 (Photo Research Spectra Spot Meter PR-1500). Background room luminance was approximately 2 cd/m^2. The monitor uses a TV raster with 60 Hz interlaced frames and the reversal rate was asynchronous with respect to this frame rate. While this caused reversal artifacts to appear on the screen, they were constant and of low contrast and low spatial frequency at the reversal rates selected. The display subtended 8.25 x 11.5 deg of visual angle at the viewing distance of 57 inches. A short viewing distance (large stimulus display) was used to maximize the VER. At 13 cycles/deg the transfer function of this display falls to about 80% of nominal contrast. Higher frequency contrast threshold determinations for both VER and psychophysically determinations will be affected equally by the monitor falloff.

Contrast $(L_{max} - L_{min}/L_{max} + L_{min})$, spatial frequency or temporal rate of alternation could be individually manipulated on a given trial by applying an external control voltage to the pattern generator. Counterphase flicker was set at either 3, 7 or 43 reversals/sec, producing cortical potentials at 3, 7 or 43 Hz respectively.

Responses. Cortical responses were recorded using a gold cup electrode placed 2.5 cm above the inion and referenced to an ear, using the contralateral ear as ground. The EEG was amplified with a Grass Model P511J AC pre-amplified (Gain, 10,000). This amplified signal was then shared by a pair of lock-in amplifiers (EG&G/PAR Ortec/Brookdeal 9505SC). The phase of the response with respect to the pattern reversal is calculated by the vector computation option of this quadrature (dual detector) instrument regardless of the particular phase relationship between the response and reference (pattern reversal) signal. In the procedure which we developed in 1981 and applied in this contract, signals from four phase sensitive detector channels at four different phases are stored in a Nicolet 1170 signal averager. The vector phase computation is used to specify (select) the optimal channel for plotting and analysis.

Experimental procedure. Contrast thresholds were estimated by sweeping contrast of a constant spatial frequency grating (0.5,1,3,4,8 or 12 cycles/deg) at one temporal rate (3,7,43 reversals/sec). Contrast increased logarithmically from 0.1% to 20% over a 20 sec trial period. A logarithmic sweep was chosen based upon the known linear relationship between neural response amplitude and logarithmic changes in contrast (Campbell & Maffei, 1970). During the sweep, subjects were instructed only to fixate a central point; no subjective responses were required.

Threshold estimation. Thresholds were estimated by extrapolating the response slope to the point at which the response first appeared. Runs were begun during periods of stability in the background EEG. At the beginning of a visually driven response (threshold), the output begins to climb regardless of its current resting voltage level. A zero response point is thus defined which determines the base line for extrapolation. This voltage may no be the electrical zero. Laboratory tests have provided a demonstration of the invariance of thresholds inferred by these methods when starting baselines are purposely selected over a wide range of starting voltage levels. This demonstration is given in Part III below.

As others have noted, a particular strength of the technique is its immunity to response amplitude fluctuations (Tyler, Apkarian, Levi & Nakayama, 1979). Amplitude changes affect the slope of the linear response, not the intercept from which the threshold is inferred. As in previous work, response slope as a function of stimulus strength has been extrapolated back to the true zero response level, although this response zero may be shifted from moment to moment away from electrical zero. The ratio of signal to average noise level has been used by others (Tyler and Nakayama, 1982), but this is more suitable to quantifying measurements of suprathreshold response strength than to threshold estimation.

Psychophysics. Psychophysically defined thresholds were obtained in separate trials for each stimulus condition. The observer was allowed to adjust the contrast of the monitor using a potentiometer. Ascending (increasing contrast to threshold) and descending limits were averaged to yield individual points on the psychophysical CSF.

Results

We have been able to define contrast sensitivity functions for 10 normal observers using lock-in retrieval of the visual evoked response (Table 1). The electrophysiologically determined CSF tracks the same process as the psychophysically determined CSF as spatial frequency and temporal rate are varied, although with a slight loss of sensitivity.

Table 1 about here.

Results from 4 subjects studied in greater detail are now described. Fig. 5 shows 12 lock-in retrieved responses for one subject at all spatial frequencies (3 reversals/sec). Using the threshold estimation method described above, CSFs were derived from such records. Variability of contrast thresholds among runs of the same spatio-temporal condition were approximately 30% for each observer (e.g., from 1.0% to 1.3%).

Table 1

VER- AND PSYCHOPHYSICALLY-DEFINED CONTRAST SENSITIVITY THRESHOLDS

observers:	1 cycle/degree VER	psychoph	4 cycles/deg VER	psychoph	7 cycles/deg VER	psychoph
experienced normals	**0.77**	0.42	**0.99**	0.50	**2.59**	0.99
(4 subjects) SD:	0.37	1.00	0.27	1.70	1.04	2.63
naive normals	**0.88**		**1.09**		**2.58**	
(6 subjects) SD:	0.43		0.27		0.61	
T-test	0.09		0.06		0.01	

Table 1. Mean VER-inferred contrast thresholds in percent for 6 naive normal observers are shown in comparison to the 4 experienced observers whose results are presented in detail in the subsequent Figures. Standard deviations are shown under each mean. All VER results were obtained at 7 reversals/sec. No difference between experienced and naive observers was significant.

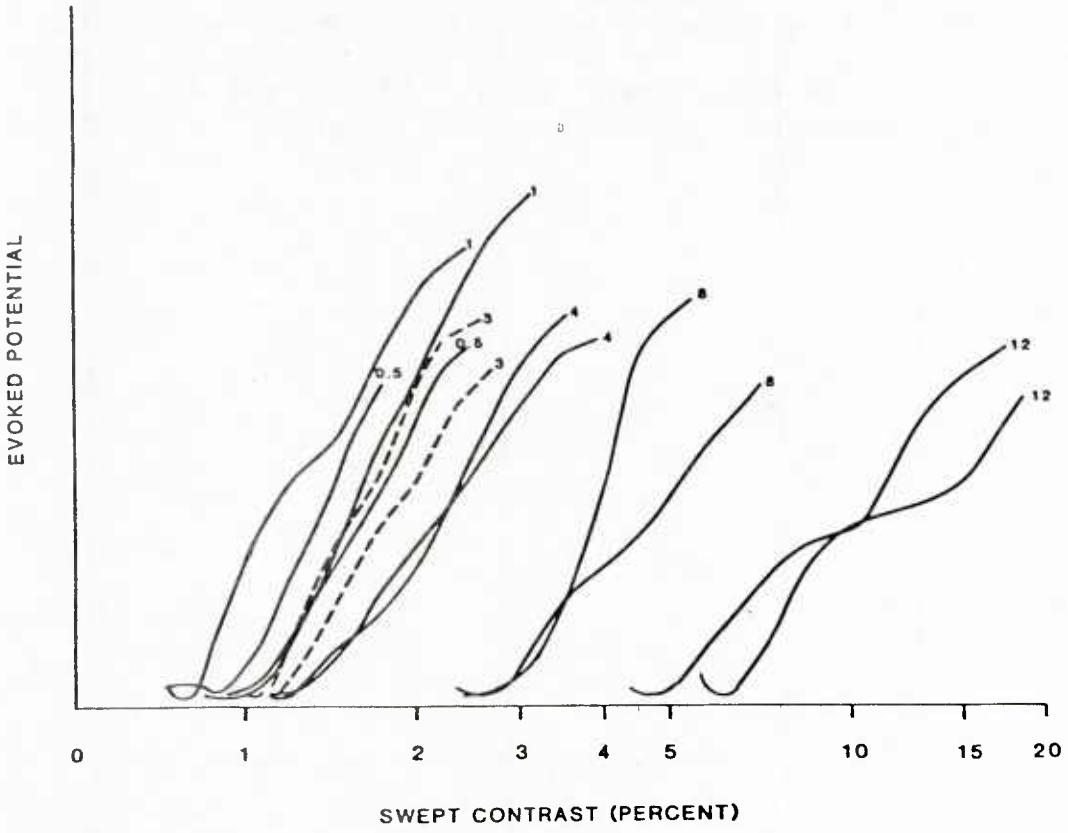


Fig. 5. An entire contrast sensitivity function is obtained with the rapid swept stimulation technique. Sample of the monocular raw data of one subject. The threshold-defining sections of twelve sweeps of contrast have been superimposed on the X-axis (contrast). In each case, contrast increased from left to right during a 20 sec run, and response climbed accordingly. The turnaround point at the toe of each curve gives the threshold. Finer gratings require more contrast to see; thresholds are higher. The grating spatial frequency for each run is given by the number above each curve. The contrast sensitivity function is defined as the contrast required for pattern detection as spatial frequency increases. Contrast sensitivity functions obtained from these and other data are shown in the following Figures.

Contrast sensitivity functions at 7 reversals/sec, as well as a comparison of the VER and psychophysical measures at this temporal frequency, are shown for four subjects in the four panels of Fig. 6. The shapes of the functions are similar for the two measures, although the VER is consistently less sensitive than the psychophysical CSF (mean of 0.4 log units less at 7 reversal/sec). The difference would be 0.15 log unit less (i.e., 0.25) if the VER thresholds were compared to only ascending psychophysical thresholds. In spite of this sensitivity loss, the VER determined CSF does appear to measure the same process. For example, subject

MK showed a sharp low spatial frequency fall-off in sensitivity at 7 reversals/sec for both the VER and psychophysical measures, whereas, subject PW did not show this fall off in either measure. One important difference between the two measures was apparent. In all subjects, the VER derived CSF showed a broader and less well defined peak than the psychophysical results.

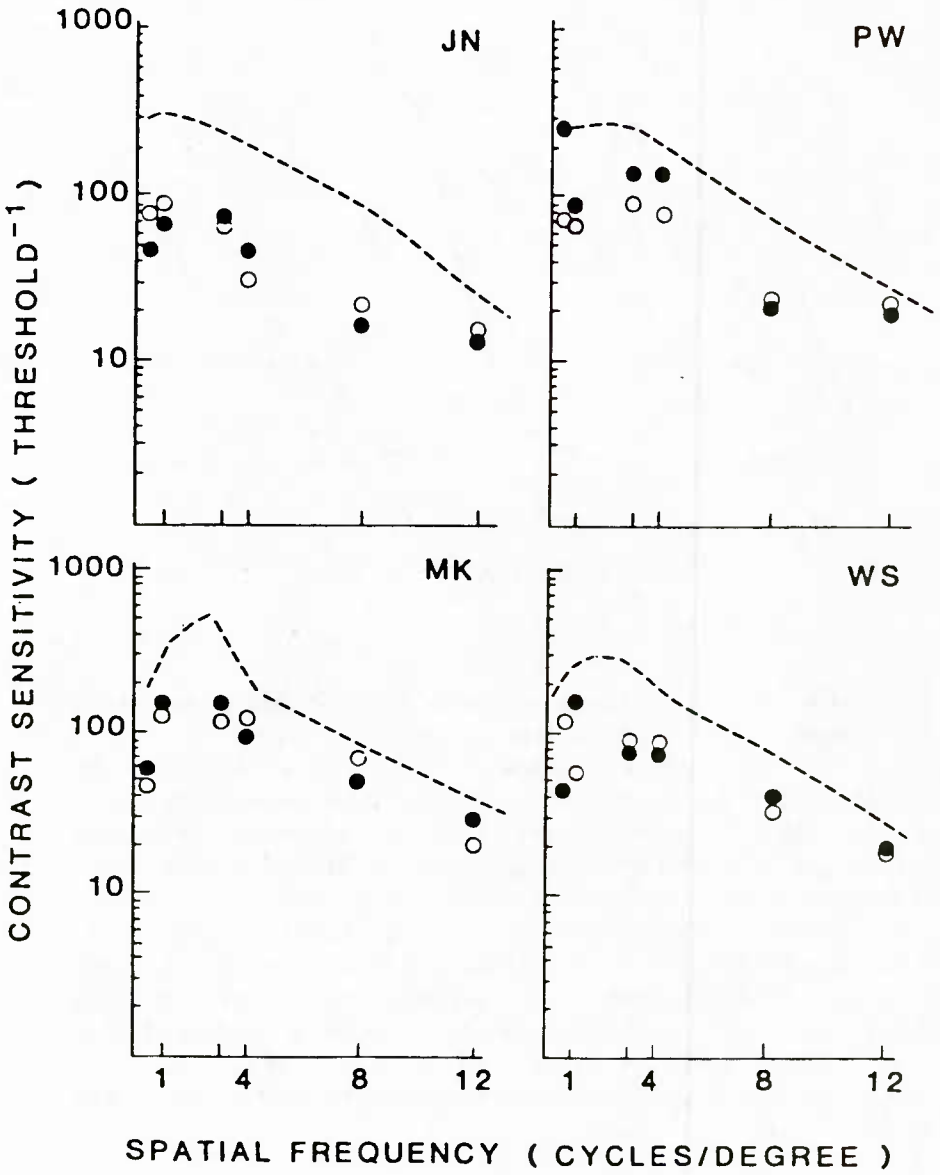


Fig. 6. Visual performance determined directly from the brain's response (**data points**) comes close to psychophysical performance (**curves**). Contrast sensitivity functions are shown for four subjects at 7 reversals/sec. ——: average of the two monocular psychophysical thresholds. **Open circles:** electrophysiologically defined thresholds for the right eye; **Closed circles,** left eye.

Monocular CSFs for two subjects are plotted in Fig. 7 with temporal rate shown parametrically. All subjects showed a loss of contrast sensitivity as rate of alternation was increased to 43 reversals/sec. Again the VER and psychophysically determined CSFs showed similar behavior. For example, subject MK exhibited the largest fall off of sensitivity at the high temporal frequency psychophysically and this loss was also reflected by the VER derived sensitivity. Subject WS showed the least fall off in sensitivity psychophysically and also showed less reduction in VER contrast sensitivity at the high temporal frequency. The other two subjects showed intermediate losses in sensitivity at the higher reversal rate, again with the psychophysics and VER results running in parallel.

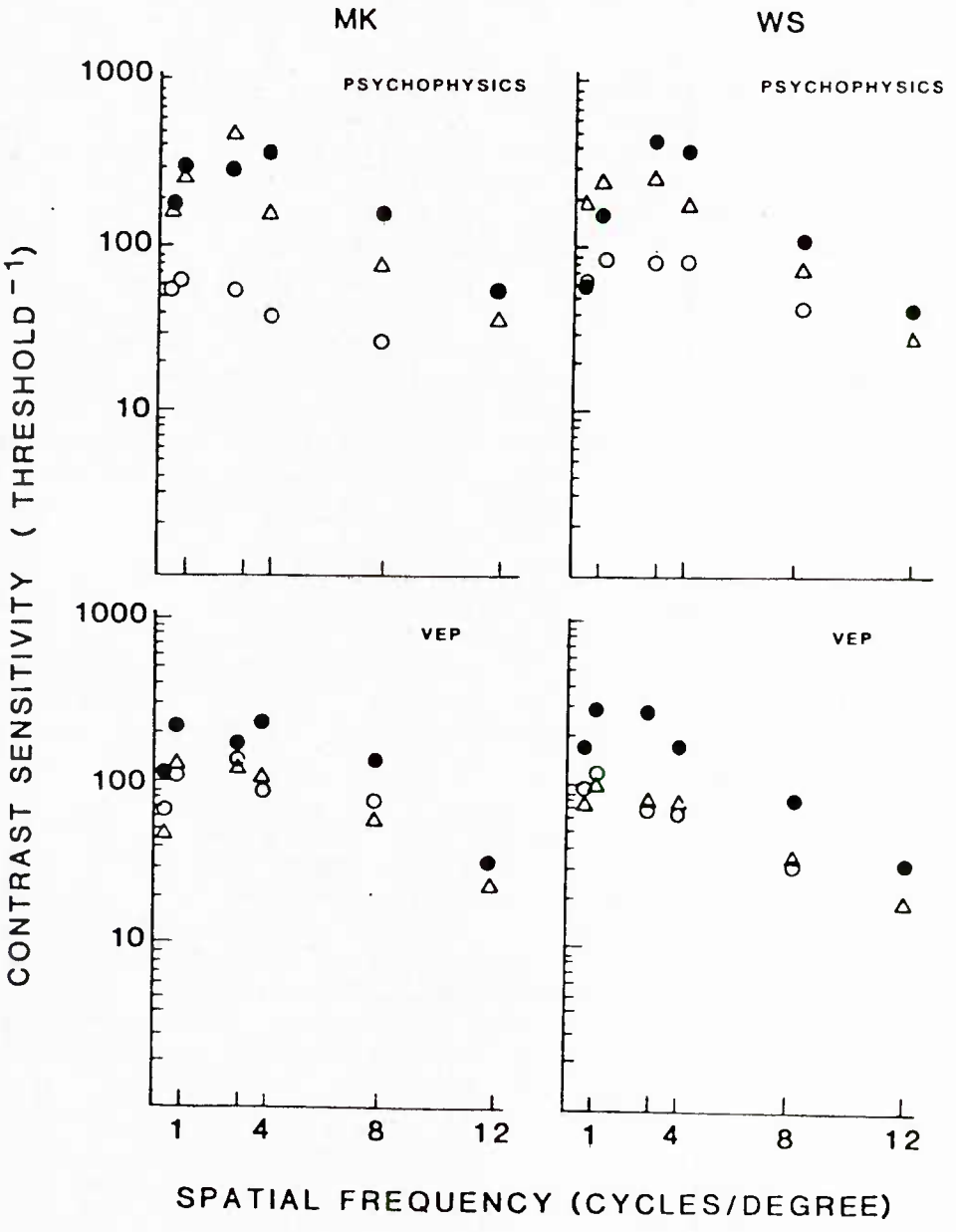


Fig. 7. Monocular electrophysiological contrast sensitivity functions of two subjects at three reversal rates. **Closed circles:** 3 reversals/sec; **Triangles:** 7 reversals/sec; **Open circles:** 43 reversals/sec.

Discussion

Contrast sensitivity thresholds may be inferred over a range of spatial and temporal frequencies from the VER using swept display stimulation and lock-in response retrieval methods. With these new techniques, a contrast sensitivity function may be measured directly from the brain's response in a few minutes of recording. Although overall sensitivity is lower, the VER-inferred thresholds correlate well with those obtained under the same conditions using standard psychophysical methods, and show variations in response to temporal and spatial frequency changes similar to those previously reported from psychophysical experiments (Robson, 1966; Kelly, 1977).

The current VSCAN method may be considered an automated version of that used by Campbell and Kulikowski (1971, 1972) with steady state responses, and by Kulikowski (1978) with transient averaged evoked potentials. In those studies, contrast thresholds were inferred for one spatial frequency at a time by extrapolating to zero a series of VER amplitudes obtained in a series of separate runs. The "extrapolation to zero response" technique makes true threshold estimation possible, and automation makes extrapolation practical. Recording response amplitude as a function of spatial frequency, while interesting in its own right, is no substitute for these methods. It is generally agreed that suprathreshold VER amplitudes have little correlation with the contrast sensitivity. Thus the curves of Tyler et al. (Tyler, Apkarian & Nakayama, 1978; Tyler, Apkarian & Nakayama, 1980) for suprathreshold VER amplitude as a function of spatial frequency show several sharp peaks rather than the smooth curve of a CSF.

On the average, the sensitivity obtained with this technique is less than one can obtain using psychophysical methods. Lower VER sensitivity could arise because the activity of fewer neurons is required to determine psychophysical thresholds than to generate an observable scalp potential (Movshon, Tolhurst & Dean, 1982). Alternatively, it may be that the mechanisms which generate a scalp potential are ancillary to the neuronal processes determining the psychophysical response.

Lock-in signal retrieval techniques are not immune to all problems inherent with the averaged VER. Although viewing time is limited to 20 sec in our experiments, adaptation effects may alter the inferred threshold (Childers, Doyle, Brinck & Perry, 1972). Two procedures were employed to reduce this: first, contrast was always swept from below threshold to above. This minimizes prior exposure to supra-threshold contrasts. Secondly, when spatio-temporal condition were repeated, orientation was alternated between horizontal and vertical orientations. The thresholds to these two orientation did not differ (Nelson, Kupersmith, Seiple & Carr, 1982) and were combined. Arousal and attention level may also influence VER amplitude, a problem which is inherent in any testing method. During long averaging periods attention varies and the recorded evoked potential amplitude reflects some average attention level. Although attention may vary even during the brief 20 sec recording period used here, departure from the anticipated linear slope is immediately evident and entire runs can be discarded. In sum, the major disadvantages of lock-in retrieval techniques appear to be the level of technical expertise needed to understand and apply them, and the variability of the data obtained.

Electrophysiologically defined contrast thresholds have heretofore been difficult to obtain in a clinical setting (Kupersmith, Nelson, Seiple, Weiss & Carr, 1983). With real-time lock-in signal retrieval of evoked potential in response to a swept contrast, a rapid and objective measure of contrast sensitivity functioning can now be obtained in naive patients. Retinitis pigmentosa patients with $\leq$ 20/50 vision have shown contrast sensitivity losses at the higher spatial frequencies using this technique. In multiple sclerosis patients, the technique is capable of resolving contrast sensitivity losses which are spotty with respect to spatial frequency, as previously detected with psychophysical techniques (Regan, Silver & Murray, 1977). These results are presented in Part V.

We hope as this method is further applied improvements will be made to improve its simplicity, sensitivity, and reliability.

PART III. THE SEPARATION OF X- AND Y-DOMINATED VISUAL EVOKED RESPONSES

As any engineer knows, one can't have everything; tradeoffs must be made. This is true for the design of a vision system, even a system with all the resources of the human nervous system. Within the visual system, the so called X and Y parallel visual pathways to the brain display tradeoffs cast in terms of spatiotemporal specialization. Where one system has fine resolution, the other is relatively coarse, as briefly reviewed below. Since the electronically swept stimulus displays of the VSCAN technique give us great freedom in testing performance for a wide range of spatiotemporal stimulus parameters, we might be able to locate stimulus settings which produce responses dominated by either the X or the Y visual subsystem alone. Such domination or purity would only be expected near threshold, since with strong stimulation, both systems respond vigorously. A tool which could isolate and access the activity of these systems in man would be an advance in visual science; it would help to specify the tradeoffs facing the visual system, and how the human visual system optimizes those tradeoffs.

How would one recognize an X-dominated response if it appeared? From basic neurophysiology, we know which stimulus conditions are relatively favorable to the X and to the Y visual subsystems. A straightforward approach would be to use the new technique to sweep from suspected X-favoring to Y-favoring conditions while seeking discrete amplitude peaks in the observed response. Preliminary results of this sort are presented. However, such results are only suggestive; interpretation is difficult. If different structures are stimulated by different stimuli, what sort of dipoles do the structures present to the electrodes? If we see two peaks, we assume there were two positive dipoles, but other possibilities exist. The two peaks could be caused by a single response mechanism, with cancellation at intermediate conditions by a second dipole which passes undiscovered. Logically, it is somewhat circular to ask which spatio-temporal conditions separate X- and Y-dominated responses, and then conclude that such response differences as are found must arise from XY differences. Some independent label of X-dominated activity is needed. For this label, we chose the oblique effect of inferior acuity and contrast sensitivity for

obliquely oriented test contours. This effect and its connection to the X system is explained briefly below.

In these oblique effect studies, we swept spatial frequency (Tyler, Apkarian, Levi & Nakayama, 1979) as well as contrast to obtain the required acuity limit and contrast threshold estimates respectively.

With fine stripes and low pattern reversal rates we were able to demonstrate the oblique effect in both contrast sensitivity and acuity limit. Low spatial frequencies and high reversal rates abolished the effect. I suggest that performance at these resolution and contrast thresholds is X-determined under spatiotemporal conditions which support an oblique effect, and Y-determined under spatiotemporal conditions which abolish the oblique effect. Evidence is reviewed that the X visual subsystem supports the oblique effect and the Y system does not. Other observations supporting this interpretation are presented.

Background on X and Y visual subsystems

The new visual duplicity. The observation that cat retinal ganglion cells can be divided into those which sum luminous flux linearly across their receptive fields and those which do not (Enroth-Cugell & Robson, 1966) has proved to be a landmark in visual neurophysiology. The central pathways and eventual cortical projections of the linear (X-type) and non-linear (Y-type) ganglion cell groups are sufficiently different to warrant referring to them as separate, parallel visual subsystems. X and Y cells go different places and do different things. These subsystems are differently specialized in both structure and function, the X to optimize spatial resolution and the Y to optimize both temporal resolution and low contrast performance with gross patterns, where acuity is not the paramount limitation on visibility (for reviews, see Stone, Dreher & Leventhal, 1979; Lennie, 1980). Many changes in perceptual performance occur when changes are made in the spatiotemporal parameters of stimulation. These changes are widely attributed to a shift between X vs. Y domination of threshold behavior. Spontaneous fluctuations in above-threshold percepts have also been attributed to competition between X and Y visual subsystems (Nelson, 1975). Here, we ask whether it is possible to directly record separate X vs. Y dominated electrical responses in man.

We turned to the VSCAN technique because it offers greater freedom to explore a range of spatial and temporal frequencies than computer averaging. Since the X and Y visual subsystems show different spatiotemporal specializations, it might be possible to isolate them simply by changing the spatiotemporal conditions of stimulation. We acknowledge that the stimulus selectivity differences between the two subsystems are not great, so that the advantage enjoyed by one system over the other can never be overwhelming. Nevertheless, if there is any advantage at all, then the system which enjoys it will make the dominant contribution to response at threshold.

Methodological details

Subjects, optics. The four subjects had normal eyes and vision correctable to 6/6. A special effort was made to correct astigmatic error at the 57" viewing distance. All astigmatism (0.5D or less in three subjects) was axis 90 or 0, so that acuity deficits from this source would be likely to occur for horizontal and vertical--not oblique--contours. It is remotely possible that acuity deficits from inaccurate optical correction would be other than horizontal and vertical (**HV**). The fact that observed HV acuities were always equal, and that there were no meridional acuity variations under appropriate spatiotemporal conditions (i.e., that we could abolish the oblique effect), both indicate that optical correction was accurate.

Response. Differential recordings were obtained between electrodes positioned 2.5 cm above the inion and the mastoid, with the body grounded through the contralateral ear. The EEG was amplified with a Grass Model P511J AC preamplifier (band pass 0.1 to 100 Hz) and the evoked potential retrieved with an EG&G/PAR Ortec 9505 quadrature lock-in using vector computation of amplitude and phase. An IOL pattern generator produced sine wave gratings on a Conrac QQA 14N/a video monitor at a mean luminance of 50 cd/m^2. Contrast was set at 75% for acuity runs. Pattern reversal was either 3 rev/sec or 43 rev/sec for all results reported here, except for the electronically swept reversal rate experiments used to explore the temporal domain. The four orientations tested were horizontal and vertical (**HV**) and right and left obliques (**RO, LO**).

Threshold estimation. The point at which the linear response slope commences defined the threshold. Unlike previous workers (Tyler, et al., 1979), we chose not to extrapolate to an absolute zero voltage baseline. A zero voltage baseline can not be used because of EEG interference. This interference can charge the integrator following the instrument's phase sensitive detector to large positive or negative values (with vector computation, only positive magnitudes can occur). The integrator is not discharged prior to a run, so that the DC level at the moment we start is seldom zero. A demonstration of threshold invariance when baselines (starting points) occur over a wide range of non-zero voltage levels is provided below.

Results

Oblique effects in both VER-inferred acuity and contrast thresholds were demonstrated, and we were readily able to identify the spatiotemporal conditions which supported or abolished the effects. A high reversal rate abolished both oblique effects. In addition, we were able to abolish the oblique effect in contrast threshold by switching to a low spatial frequency.

Swept contrast. VER-inferred contrast thresholds ranged from 0.75% to 2.0% for vertical and 0.65% to 2.0% for horizontal, 4 cycles/deg sine wave gratings temporally modulated at 3 reversals/sec. We would expect these HV thresholds to be similar. HV stimulus contrast thresholds differed by 0.1% or less for each subject. The contrast thresholds obtained for right and left oblique gratings ranged from 2.45 to 5.0% and 2.7 to 6.35% respectively (Fig. 8). The difference in thresholds between the two oblique orientations

was 1.35% or less. The significant comparison is between HV and oblique orientations. The oblique effect is shown by the fact that the mean contrast threshold for HV gratings was superior by 2.2% or more to oblique stimulus thresholds in each subject.

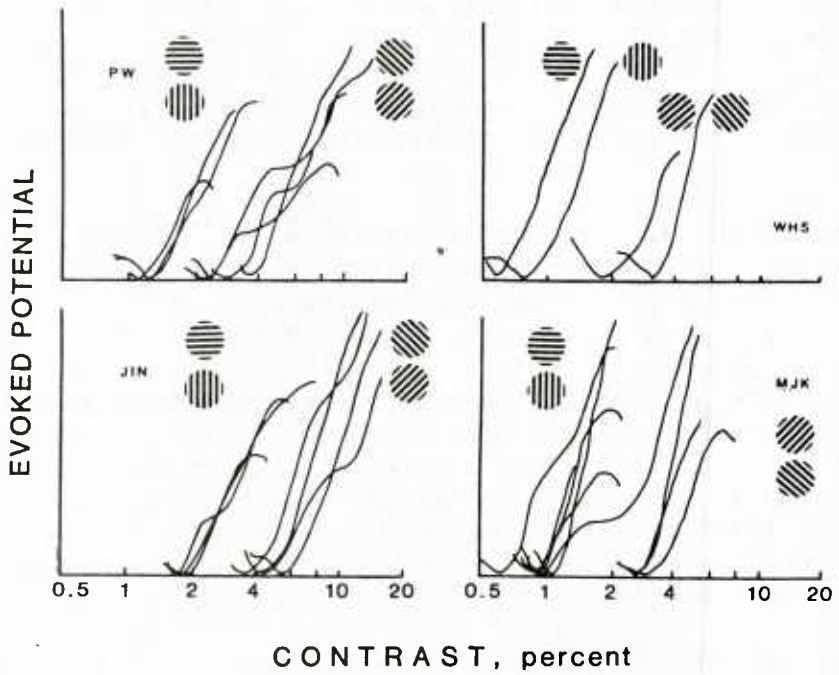


Fig. 8. Visual performance is known to be poorer for obliquely oriented stimuli, and this may be seen directly in the brain's response. Oblique effect in contrast threshold for four observers. Contrast of a 4 cycle/deg sine wave grating was swept in 20 seconds from 0.5% to 20% contrast while alternating at 3 rev/sec. For each observer, all HV runs have lower (better) thresholds than oblique runs, so that curves fall into two groups, all members of which are HV and oblique respectively. Eleven replications are shown. Exact values are given in Table 2. The X-type visual subsystem may be responsible for this effect.

With spatial frequency at the original value of 4 cycles/deg, but temporal modulation increased to 43 reversals/sec, the oblique effect was abolished. The vertical and horizontal stimulus thresholds were again similar, ranging from 0.6 to 1.23% and from 0.61 to 1.52% respectively (Fig. 9). The difference in VER-inferred thresholds between HV orientations was less than 0.3% for all subjects. The VER-determined thresholds for oblique gratings ranged from 0.66 to 1.2% and from 0.7 to 1.05 for right and left obliques respectively. The difference in the thresholds for these two orientations was less than 0.18% for each subject. Again, average HV vs. oblique threshold is the comparison of interest. This difference was less than 0.04% in three subjects (no oblique effect) and 0.23% (90% reduction) in the fourth. High temporal frequency abolished the oblique effect.

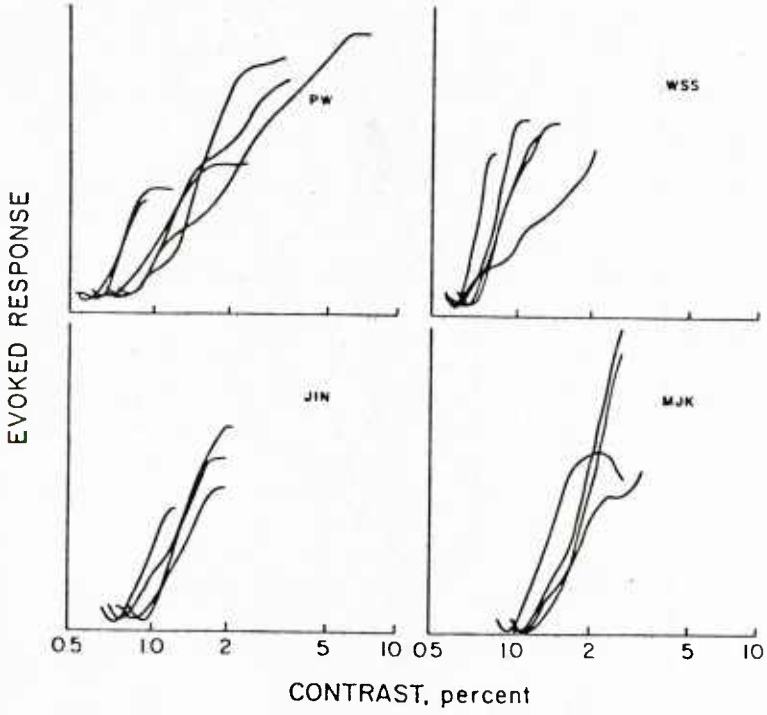


Fig. 9. The oblique effect is abolished for four observers when the temporal frequency is increased to 43 rev/sec. Stimulus and sweep otherwise as in Fig. 4. Note that absolute contrast sensitivity is undiminished. Exact threshold values are given in Table 2. Because the oblique effect is absent, the X-type response may be relatively weak under these spatiotemporal conditions, causing the observed potentials to be dominated by the Y visual stream.

Table 2 about here.

We returned to the 3 reversal/sec temporal frequency which supported the oblique effect, but lowered the spatial frequency. With coarse gratings of 1 cycle/deg, contrast threshold estimates were minimally changed to a range of 0.69 to 0.76% and 0.69 to 0.73% for vertical and horizontal orientations respectively (difference between HV stimulus thresholds was less than 0.07% in each observer; Fig. 10). However, there was a marked improvement of the contrast threshold estimates for obliquely oriented gratings. These thresholds ranged from 0.62 to 1.17% for the right oblique and 0.58 to 1.20% for the left oblique (difference in any one observer less than 0.13%). Thus, the oblique effect was abolished by low spatial frequency stimulation: the HV oblique difference was slightly reversed from an oblique effect or less than 0.1% in 3 observers, and only 0.45% in the fourth.

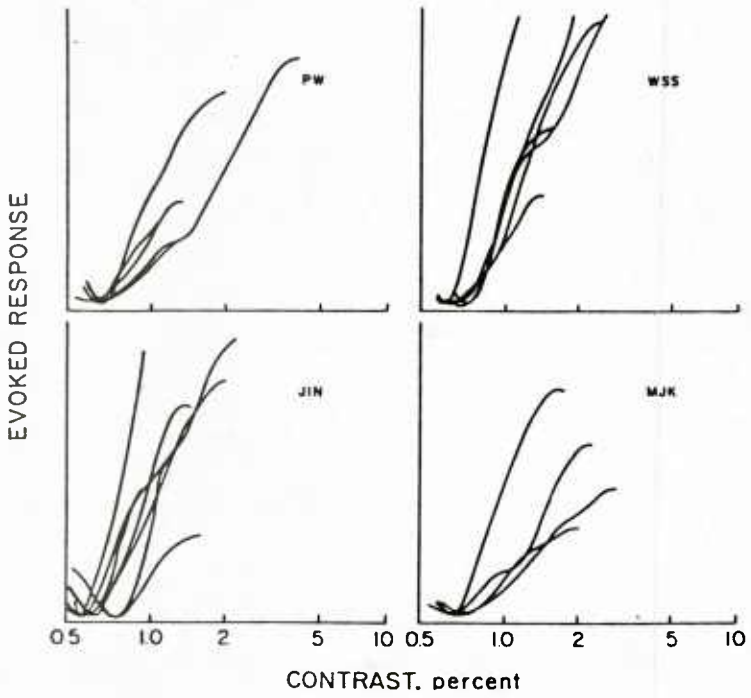


Fig. 10. The oblique effect is abolished for four observers when the spatial frequency is lowered to 1 cycle/deg. Stimulus and sweep otherwise as in Fig. 4. Six replications are shown. Exact threshold values are given in Table 2.

COMMENT: Contrast thresholds for an obliquely oriented 4 cycles/deg grating reversed three times a second were elevated 2.5 to 4.3 times the thresholds of either horizontal or vertical gratings (up to 0.6 log units) in normal observers. This is comparable to the thresholds shifts reported by Maffei & Campbell (1970; 0.3 log unit) and by Zemon, Gutowski & Horton (in press; 0.2 log units) using conventional fixed parameter stimuli and discrete trial computer averaging techniques. Either lowering the spatial frequency by two octaves or increasing reversal rate to 43 times a second eliminated this oblique effect in contrast sensitivity by eliminating the sensitivity deficit for oblique orientations.

Swept spatial frequency: acuity limit. The electrophysiologically-determined acuity limit ranged from 15.9 to 18.6 cycles/deg for vertical, and 14.5 to 19 cycles/deg for horizontal sine wave gratings reversing 3 times a second (Fig. 11). Except in one case, HV acuity threshold estimates differed by less than 1 cycle/deg. The acuity thresholds for right and left oblique stimuli ranged from 10.9 to 17.6 cycles/deg and 11.3 to 17.7 cycles/deg, respectively. The difference in thresholds between the two oblique orientations was less than 1.3 cycles/deg in all four cases. The significant comparison arises between the average of HV thresholds and the average of right and left oblique thresholds. HV acuity always exceeded oblique acuity--an oblique effect. This difference was greater than 2 cycles/deg in 3 cases (approx. 0.1 octave); the fourth observer's difference was 1.2 cycles/deg.

Table 2

THE OBLIQUE EFFECT IN ACUITY AND CONTRAST SENSITIVITY

ACUITY, cycles per degree, at 3 rev/sec:

	vertical	horizontal	VH mean	diff	R/LO mean	RO	LO
PW	16.67	14.50	15.58	3.45	12.13	12.08	12.19
WHS	15.9	16.5	16.20	5.71	10.49	10.09(2)	11.3
JIN	18.58	19.0	18.79	1.17	17.62	17.6(2)	17.68
MJK	17.2(2)	16.27(2)	16.74	1.98	14.76	15.24(3)	14.04(2)
		grand mean	16.82	3.08	13.75		

ACUITY, at 43 rev/sec:

	vertical	horizontal	VH mean	diff	R/LO mean	RO	LO
PW	10.07	10.35(2)	10.26	0.62	9.64	9.87	9.42
WHS	9.67	9.22	9.44	0.03	9.41	9.22	9.6
JIN	9.76(2)	9.51(2)	9.63	-0.27	9.90	9.63(2)	10.17(2)
MJK	12.08(2)	12.62(2)	12.35	-0.33	12.68	13.03(2)	12.33(2)
		grand mean:	10.42	0.01	10.41		

CONTRAST THRESHOLD, percent, 3 rev/sec at 4 cpd:

	vertical	horizontal	VH mean	diff	R/LO mean	RO	LO
PW	1.20	1.19(2)	1.19	1.79	2.98	3.25(2)	2.71(2)
WHS	0.75	0.65	0.70	2.32	3.02	2.45	3.60
JIN	2.0	2.0	2.0	3.68	5.68	5.0(2)	6.35(2)
MJK	0.94(3)	1.1(3)	1.02	2.21	3.23	3.05(2)	3.60
		grand mean:	1.23	2.50	3.73		

CONTRAST THRESHOLD, 3 rev/sec at 1 cpd:

	vertical	horizontal	VH mean	diff	R/LO mean	RO	LO
PW	0.76(2)	0.69(2)	0.73	0.45	1.18	1.17(2)	1.2(2)
WHS	0.68	0.76	0.72	-0.02	0.70	0.74(3)	0.64(2)
JIN	0.67(2)	0.76	0.70	-0.10	0.60	0.63(2)	0.58(2)
MJK	0.66	0.73	0.69	0.01	0.70	0.66	0.74
		grand mean:	0.71	0.08	0.79		

CONTRAST THRESHOLD, 43 rev/sec at 4 cpd:

	vertical	horizontal	VH mean	diff	R/LO mean	RO	LO
PW	0.64(2)	0.79	0.69	0.03	0.72	0.66(2)	0.83
WHS	0.76(2)	0.61(2)	0.68	0.03	0.71	0.73(2)	0.70(2)
JIN	0.66	0.94	0.80	-0.02	0.82	0.86	0.79
MJK	1.23	1.52	1.37	-0.25	1.12	1.20	1.05
		grand mean:	0.89	-0.05	0.84		

KEY: VH=vertical/horizontal; R/LO=right/left oblique.
(N)=average of N runs; 42 replications total.

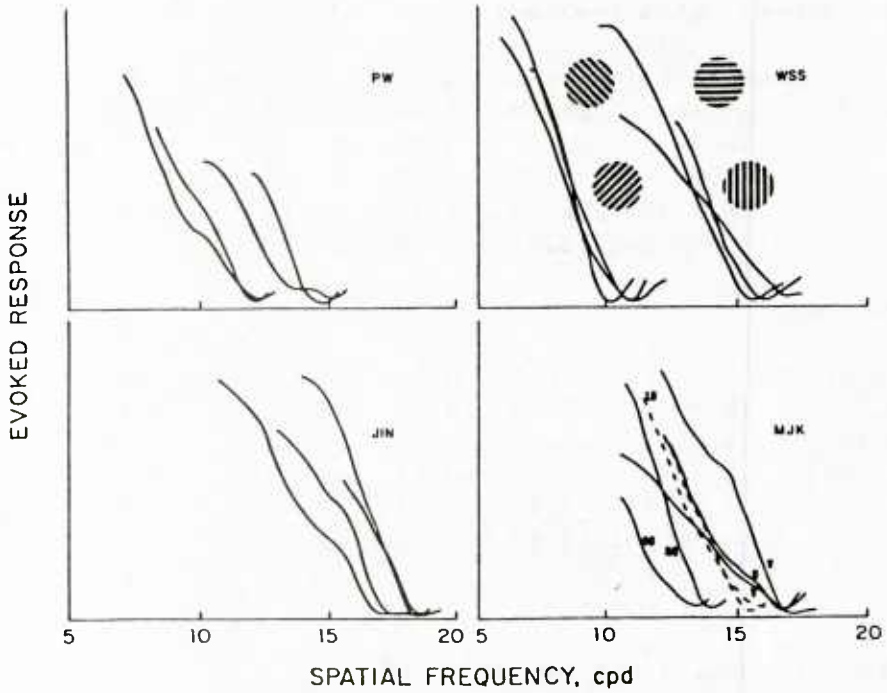


Fig. 11. Oblique effect in acuity for four observers. Spatial frequency of sine wave grating was swept in 20 seconds from 5 to 20 cycles/deg for four grating orientations (horizontal, vertical, right and left obliques). Contrast, 75%; 3 rev/sec, square wave temporal modulation. The upper spatial frequency cutoffs were always lower for oblique than for horizontal and vertical orientations. Replications are shown for some orientations. Subject MJK: curves in order of ascending acuity are right oblique (RO), left oblique (LO, dashed lines), and horizontal-vertical (HV; V replicated). Note that all HV curves for this subject indicate the same threshold even though the slope varies. Precise threshold values for all subjects are tabulated in Table 2.

An oblique effect could not be demonstrated at 43 reversals/sec. VER-inferred horizontal and vertical (HV) acuity thresholds ranged from 9.2 to 12.6 cycles/deg and from 9.7 to 12.1 cycles/deg respectively (Fig. 12). At this reversal rate, the difference between horizontally and vertical driven VERs was less than or equal to 0.5 cycles/deg in each subject. For right and left oblique stimuli, the acuity thresholds ranged from 9.2 to 13.0 cycles/deg and 9.4 to 12.3 cycles/deg respectively. Within-subject differences in threshold estimates were less than 0.7 cycles/deg in all cases. On average, the difference in HV vs. oblique thresholds was less than 0.7 cycles/deg.

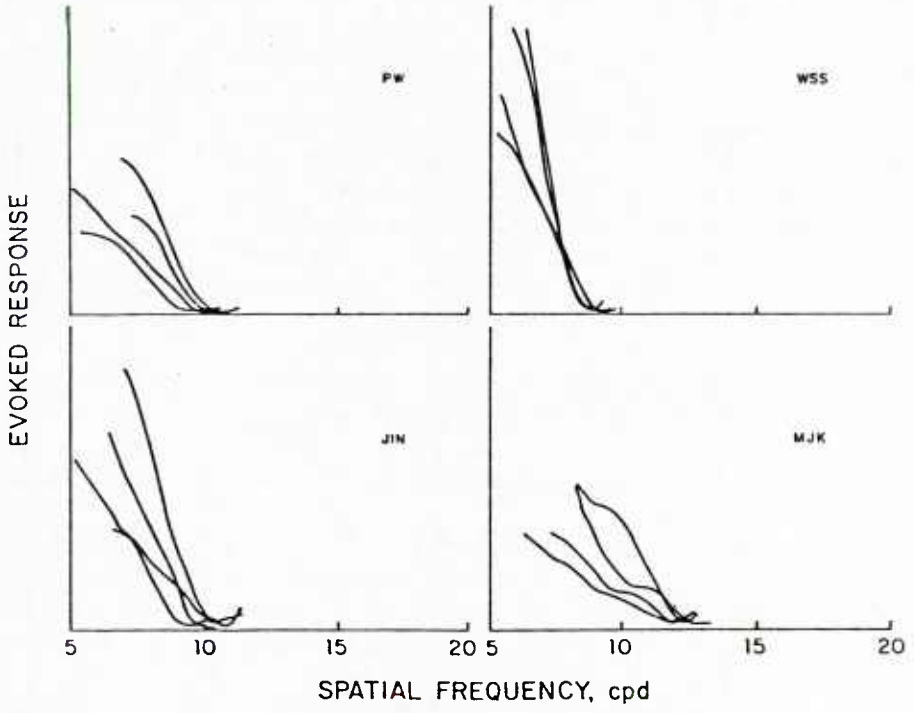


Fig. 12. The oblique effect in acuity is greatly diminished for four observers when the pattern reversal rate is 43 reversals/sec. This reversal rate also produces a general lowering of the spatial frequency limit. Stimulus and sweep as in Fig. 2. Subject PW shows a slight oblique effect (order of orientations: left oblique, right oblique, vertical, horizontal), but there is no consistent pattern among the remaining three subjects, and no HV superiority in the overall mean. Sequence of exact threshold values is given in Table 2.

COMMENT: Superior acuity for HV-oriented contours could be demonstrated electrophysiologically at a pattern reversal rate of 3 times a second. At a temporal modulation frequency of 7 reversals/sec, additional data not presented here showed the electrophysiologically measured oblique effect to be marginal from observer to observer. The oblique effect was abolished at 43 reversals/sec. The acuity limit was decreased for all orientations at 43 reversals/sec.

Discussion.

The oblique effect can be readily demonstrated with electrophysiologically-inferred contrast and acuity thresholds in man, provided temporal frequencies are low and spatial frequencies are high. These are spatiotemporal conditions which favor a dominant contribution from the X visual subsystem. Higher reversal rates and low spatial frequencies, conditions which are optimal for the Y visual subsystem, abolish the oblique effect in the evoked potential. Our hypothesis is that spatiotemporal conditions may be specified for which the X or the Y system will determine **threshold** behavior, even though both systems work together above threshold. Those

spatiotemporal conditions include the ones we have identified above as supporting or abolishing the oblique effect.

Using the oblique effect as a marker for X system activity may be an initial means of measuring the integrity of X and Y systems in a clinical setting. Current evidence that the X system is indeed the substrate for the oblique effect are briefly reviewed below. The evidence is not yet conclusive and further corroborative data must be sought. In any event, what is already known from animal neurophysiology about slightly different functional specializations, central projections and other differences suggest additional properties which should differ between putative X- and Y-dominated spatiotemporal conditions.

Neurophysiological substrate for the oblique effect. Plentiful, suggestive evidence points to the identification of steady-state potentials evoked at low temporal and high spatial frequencies with an X-dominated generator. This evidence is both neurophysiological and psychophysical.

The superior sensory coding and lower absolute thresholds for HV contours seen in the oblique effect could both be accounted for if orientation-selective neurons with horizontal and vertical optimal stimulus preferences occurred in greater absolute numbers than neurons with oblique tunings (HV bias hypothesis). Support for this hypothesis is available for monkey, which displays an oblique effect (Bauer, Owens, Thomas & Held, 1979; Boltz, Hanverth & Smith, 1979). We are concerned here not merely with whether a biased population was found, but with the classificatory criteria, if any, which set the biased population apart from other cortical neurons.

An HV bias has been shown in monkey among simple cells in the foveal projection (central 2 deg) by Mansfield (1974). Mansfield analyzed only one cell from each of 192 regularly-spaced electrode penetrations. By marching all over the cortical surface this way, Mansfield hoped to avoid sampling bias from the well-known sequence-slab (Hubel & Wiesel, 1974; Albus, 1975) and iso-slab (Hubel, Wiesel & Stryker, 1977, 1978) columnar organization of the orientation domain. In iso-slabs, for example, neurons with similar orientation tunings occur together, so that large numbers of neurons with one particular orientation preference would be encountered. Preference for high spatial frequency and foveal receptive field position defined the HV-biased population reported by De Valois, Yund & Hepler (1982). These findings have been corroborated with a local evoked potential study (Mansfield & Ronner, 1978) and extended to the cat (Bonds, 1982). The significance of using evoked potentials in animals is that the coarser implanted electrode gives a broad sampling area, and electrode sampling bias is minimized. Again in cat Albus (1975) has shown a weak HV bias among 410 cells without regard to class or eccentricity; a stronger bias among central area 17 simple cells without hypercomplexity has been reported by Kennedy & Orban (1979; full report in Orban & Kennedy, 1981), confirming the early report of Pettigrew, Nikara & Bishop (1968), who noted the bias was strongest for simple, unimodal, directionally-selective cells near the area centralis. Kennedy & Orban (1979) point out that the observation of an HV bias confined to one cell class could not be caused by an orientation column sampling bias in the electrode penetrations; an electrode sampling bias would be expected to impose an HV bias upon all classes of cells isolated. The HV bias reported by Leventhal & Hirsch (1977) was observed for central cells (within 10 deg of area centralis) which had small receptive fields and

preferred slow stimulus velocities (cutoff below 50 deg/sec). These cells were presumed to have dominant X-input. The most thorough study of orientation bias in cat striate cortex is that of Payne and Berman (1983), based on a sample of over 360 neurons. Cells with small receptive fields had the most pronounced bias, although other biases were also observed, notably a tendency for cells with receptive fields at the horizontal and vertical meridians to have vertical and horizontal optimal tunings respectively. Behavioral evidence of an oblique effect in cat is now also available, although this appears to be confined to discrimination of orientation differences (Vandenbussche & Orban, 1980) without general effects on contrast threshold (Bisti & Maffei, 1974) or acuity and spatial frequency discrimination (Vandenbussche & Orban, 1981).

Are the cells which bring us the oblique effect IN the X stream? It was shown above that neurophysiologically there is a cell population which supports the HV bias hypothesis of the oblique effect. The weakness in current neurophysiological data lies in identifying these cells as X or Y innervated. "Simple-type neuron" can not be equated with "X" (Mustari, Bullier & Henry, 1982). Unfortunately, at this time there are no generally accepted means for classifying a unit as to X, Y or mixed innervation on the basis of response to visual stimulation, and indeed classificatory schemes for cortical neurons are not completely agreed upon (Henry, 1977). Nevertheless, the appropriately biased population prefers stimulus conditions which match the conditions under which the oblique effect is observed in man, These stimulus preferences are also the ones which would be expected for cells with a strong X-type innervation.

Other evidence for XY separation at threshold. Apart from the question of the oblique effect's origin, certain stimulus conditions may favor X or Y response by catering to the two systems' different spatiotemporal preferences. In cat, the Y system can be selectively damaged by monocular deprivation; temporal sensitivity loss is then greatest at high frequencies in both the lateral geniculate nucleus and visual cortex (Jones & Berkley, 1982 in press). More telling, cat LGN Y cells always show greater contrast sensitivity at low spatial frequencies, where only X-cell sensitivity rolls off. X cells also have slightly higher absolute sensitivities when spatial frequencies are high and temporal frequencies are low (Lehmkuhle, Kratz, Mangel & Sherman, 1980; reviewed in Sherman, 1982). Under these circumstances, local response at threshold must be exclusively Y- or X-determined, respectively. Therefore, I suggest that the evoked potential may also be Y- or X-dominated at threshold. The above-threshold situation will be different. Even though X and Y paths enjoy initially segregated cortical projections in monkey (Lund & Boothe, 1975; recently reviewed by Gilbert, 1983), pure X or Y potentials above threshold seem improbable. Both systems would be active, and some cortical areas must receive convergent input. Evoked potentials would be mixed. Further, we do not know where along cortical pathways the evoked potential is generated.

Other studies of the oblique effect's spatiotemporal limits. In man, the oblique effect has been demonstrated electrophysiologically by Maffei & Campbell (1970), who did not explore the spatiotemporal conditions which elicit or abolish it. Using a single reversal rate, Adachi & Chiba (1979) observed oblique effects in evoked potential amplitudes only at spatial frequencies of 4 cycles/deg and above. Until now, the only studies of the spatiotemporal limits of the oblique effect have been psychophysical.

Psychophysically, abolition of the oblique effect for contrast has been reported for a reversal rate of 8/sec (15 cycles/deg grating, sine or square wave modulation produced identical results; Camisa, Blake & Lema, 1977). Trained observers can readily make a phenomenological distinction between pattern and motion percepts at threshold. The pattern threshold (thought to be an X-determined behavior) was always lower, and it was reported that switching to a motion threshold abolished the oblique effect. The oblique effect is absent in peripheral vision (acuity threshold; 8 deg eccentricity and beyond), and at spatial frequencies below about 4 cycles/deg (contrast threshold; Berkley, Kitterle & Watkins, 1975), both Y-favoring conditions. Two to four cycles/deg, which is the transition region between abolition vs. support of the oblique effect, is also the crossover point for flicker/motion vs. pattern channel-dominated thresholds (Green, 1981).

A Y-generated peak at 43 reversals/sec

Corroborative studies are under way to substantiate our interpretation. Perhaps the most direct indication of separate underlying generators would be the observation of distinct amplitude peaks when sweeping the spatial or temporal domains (Tyler, Apkarian & Nakayama, 1978; Nakayama, Mackeben & Sutter, 1980).

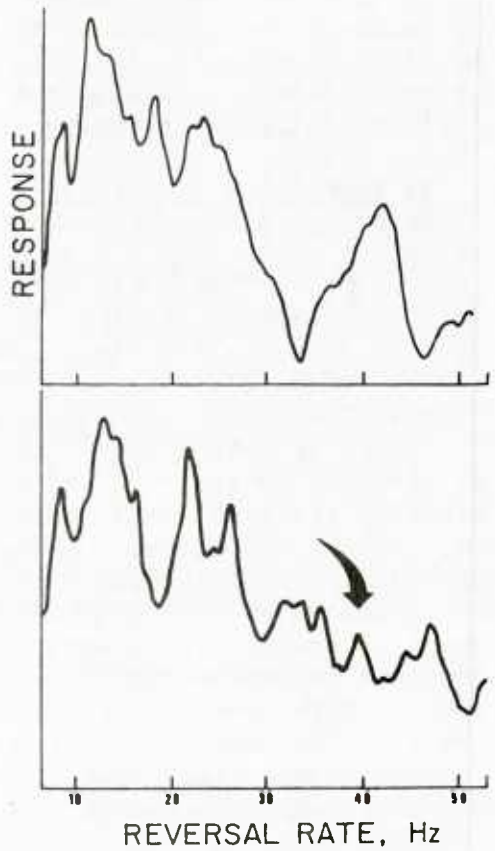


Fig. 13. Discrete potential generators at different temporal frequencies? Swept reversal rate reveals a response peak at 43 rev/sec with coarse sine wave grating (top; 1 cycle/deg, 60% contrast). Peak disappears at 10 cycles/deg (bottom, **arrow**). This result has been reliably obtained in four consecutive observers. Vector computation from quadrature phase sensitive demodulators, 3 sec time constant, 50 sec sweep duration.

We swept reversal rate over the range from 6.5 to 53 reversals/sec. We did in fact observe large, irregular amplitude peaks at reversal rates between 8 and 18 reversals/sec (Fig. 13, top), but these amplitude peaks persist in the absence of visual stimulation, are larger with eyes closed and/or eyes rolled upwards (Mulholland & Evans, 1965), and smaller if the subject is given a mental arithmetic task, all manipulations known to vary the alpha rhythm. Clearly the EEG is a major contributor to this activity and is obscuring any discrete, visually driven amplitude peak which might occur in this frequency band, unless special Fourier technique are used (Srebro, Sokol & Wright, 1981).

While EEG noise in the alpha band hampers any attempt to document a discrete X-dominated peak, at 43 reversals/sec second smaller peak was found in 4 observers at a spatial frequency of 1 cycles/deg (Fig. 13, top right). This peak disappeared with finer gratings (Fig. 13, bottom, 10 cycles/deg) and in the absence of visual stimulation. Thus, the peak is visually driven, occurs at high temporal frequencies, and depends on the presence of patterns with coarser spatial frequency content. We also stimulated with a diffuse stroboscopic flash (Grass PS-22 with additional diffusion on flash tube face, 10 deg angular subtense, lowest intensity setting). The flash rate was swept from 1.4 to 52.1 flashes/sec; electrodes at Oz and O_2, contralateral ear grounded). This patternless stimulation produced a peak similar to that observed with pattern reversal stimulation. The peak is shown in replicated runs for two observers in Fig. 14. With static pattern added to the strobe face, the peak disappears; with no visual stimulation at all, the baselines (control) activity level is lower still. Essentially similar results were obtained with sinusoidally modulated red light instead of strobe flashes.

A similar peak has been reported by Regan (1968), who noted a shorter latency and separate cortical locus for activity in this frequency region. Response non-linearity (frequency doubling) was also demonstrated. A similar temporal frequency peak has also been reported by Tyler, Apkarian and Nakayama (1981), who noted a shift toward higher optimal temporal frequencies with more peripheral visual field stimulation. This is strong circumstantial evidence that the peak is Y-generated: it depends on low spatial and high temporal frequency stimulation, it is non-linear, and, like the Y stream which has greater relative weighting in the visual field periphery and projects heavily to extrastriate areas, the peak has a different scalp locus and more Y-like temporal tuning in the periphery.

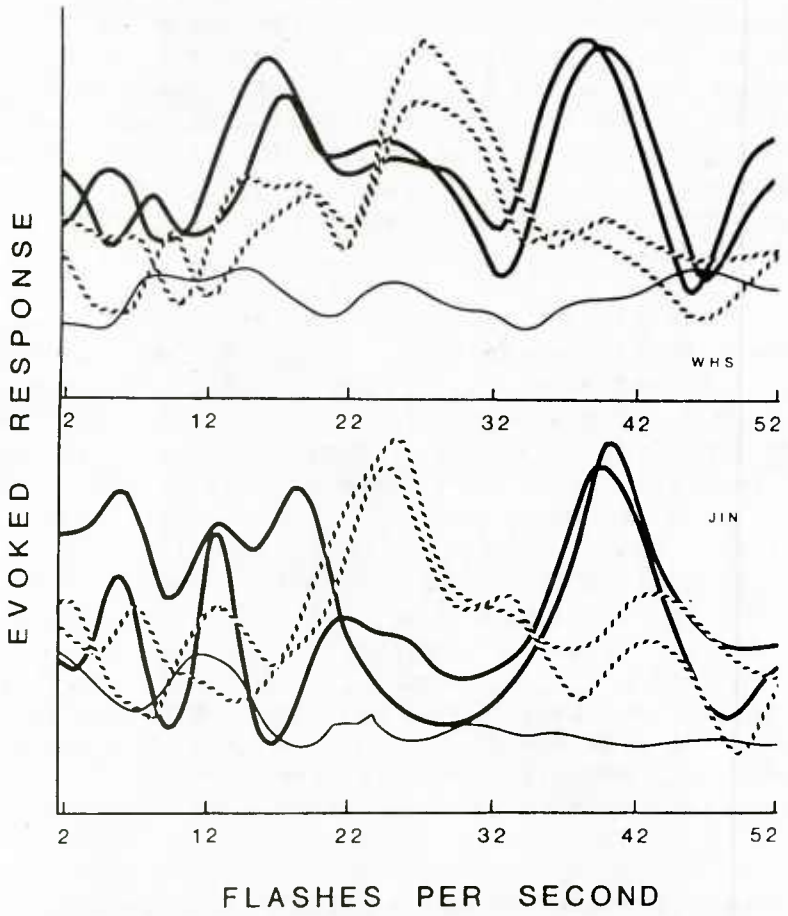


Fig. 14. Strobe stimulation, rather than pattern reversal, as in previous Figure. Swept temporal stimulation rate reveals a response peak at 40 rev/sec with blank field strobe stimulation (**solid lines**; replicated runs are shown for each condition in two subjects; top, WHS; bottom, JIN). This peak disappears when a 7 cycles/deg grating pattern is affixed to strobe face (**dashed curve**). The peak does not occur in the resting EEG spectrum (**fine line** at bottom). X axese indicate electrical zero level.

The distinction which we have chosen to draw in physiological, XY terms may well parallel the widely recognized distinction between luminance and pattern response mechanisms in the evoked response (see review in Regan, 1981, esp. his Figs. 15 & 16). If the above peak is due to a separate generator, then inferred visual performance measured under these spatio-temporal conditions should show different threshold properties. And that is what we have shown with the oblique effect.

These methods promise to transform the evoked potential into a rapid, objective measure of visual performance across the entire spatiotemporal domain. In particular, the technique promises to have great utility in clinical diagnosis, where contrast sensitivity testing is finding widespread

use (Arden, 1978), objective measures of acuity are needed (Regan, 1977; Tyler, et al., 1979), and orientation and spatial frequency selective visual losses (Regan et al, 1980) require tests too numerous to perform with conventional psychophysical techniques.

PART IV. THE INTRUSION OF EEG NOISE UPON VISUAL RESPONSES AND RESPONSE BASELINES

The third goal of the past contract period was to identify the intrusive effects of EEG noise on VSCAN recordings. Since no new means of improving signal to noise ratio could be discovered, the strategy adopted was to improve our criteria for evaluating such records as we could obtain. This work is part of a general effort to resolve controversies surrounding the swept technique (Regan, 1980; Tyler, Nakayama, Apkarian & Levi, 1981).

EEG Interference

The evoked potential must be retrieved against a background of noise which is not random. Quite the contrary, the electroencephalogram (**EEG**) exhibits bursts of activity often concentrated around one frequency and lasting several seconds. These bursts can pass the frequency selective barriers erected by lock-in techniques and appear as a response, as others have lamented (Bostrom, Keller & Marg, 1978).

EEG phase is random. Fortunately, the phase of EEG interference is random with respect to the reference, varying from moment to moment (Regan, 1966). This is illustrated in the response amplitude tracings of Fig. 15 which was obtained in the absence of visual stimulation (eyes closed). Note that the baseline is anything but flat. Two phase sensitive detector (**PSD**) channels are shown, based on identical frequency references (11 Hz) separated 90 deg in phase. The two prominent peaks are interpreted as separate 11 Hz alpha bursts, the second occurring 13 sec after the first. Whereas the phase of an evoked response is fixed, the EEG retrieved here occurs first on one channel, then on another 90 deg away. If an evoked response were being retrieved with vector computation during this episode of EEG activity, both EEG peaks would have marred the true response. With PSD, both noise (EEG) peaks could not appear at full strength on one response channel. W the reference phases chosen for this illustration, the EEG noise peak is in fact almost completely rejected. When interference phase is random, some interference must be rejected.

In the ideal case where noise is "white" (fully random), an improvement in signal to noise ratio can be realized with PSD methods. As noise becomes more narrow-band, as with an EEG alpha burst for example, this advantage diminishes. The loss in PSD superiority may be quantified by taking the autocorrelation of an EEG sample. Whereas autocorrelation of white noise yields an impulse function of zero width, the "pinkness" (frequency narrowness) of the EEG produces a broadened peak in the autocorrelation function. The reduction of the theoretical advantage of PSD over vector retrieval is on average proportional to the integral of this broadened autocorrelation peak. Thus, with the EEG, there would seem little to gain

from PSD methods. But in fact, PSD retrieval is advantageous compared to vector computation. When the noise phase is fortuitously 90 degs to the visually driven response, the noise will be completely rejected (Fig. 4). However, noise rejection on successive runs will vary with the random variations in the EEG's phase. By retrieving many phases simultaneously, it is often possible to find a channel with good noise rejection and enough residual signal to determine threshold (see "Choice of phase" below).

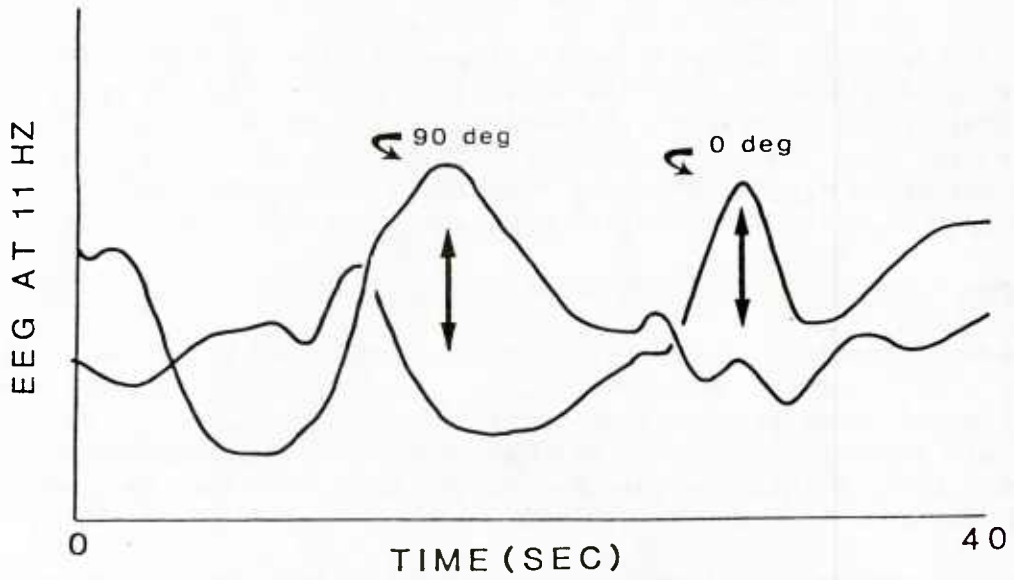


Fig. 15. In the absence of above-threshold visual stimulation, the phase of the EEG is random. Subject was seated in lit room with grating stimulator extinguished. EEG at 11 Hz was retrieved simultaneously at two phases 90 deg apart. When activity appeared on one channel, is was absent on the other, and the active channel varied from moment to moment (**arrows**).

Rise after threshold. Since EEG interference can not always be rejected, it is important to recognize its intrusions upon responses. One such intrusion is a rise in "response" at the end of a downward sweep, after a stimulus is beyond threshold. At this time, the stimulus is too faint to evoke a response, and the amplitude rise can not be visually driven. Our hypothesis was that subjects lost attention when they could no longer see anything, and consequently spontaneous EEG noise increased, analogous to the increased EEG synchronization observed at the time of stabilized image fading (Lehmann, Beeler & Fender, 1965). It is also reported that with sustained attention and sleep deprivation, photic stimulation is more likely to provoke alpha-like activity than to cause the classic blocking (desynchronization) reaction (Morrell, 1966). If the rise after threshold is due to EEG activity, it should bear no consistent phase relationship to a previous response.

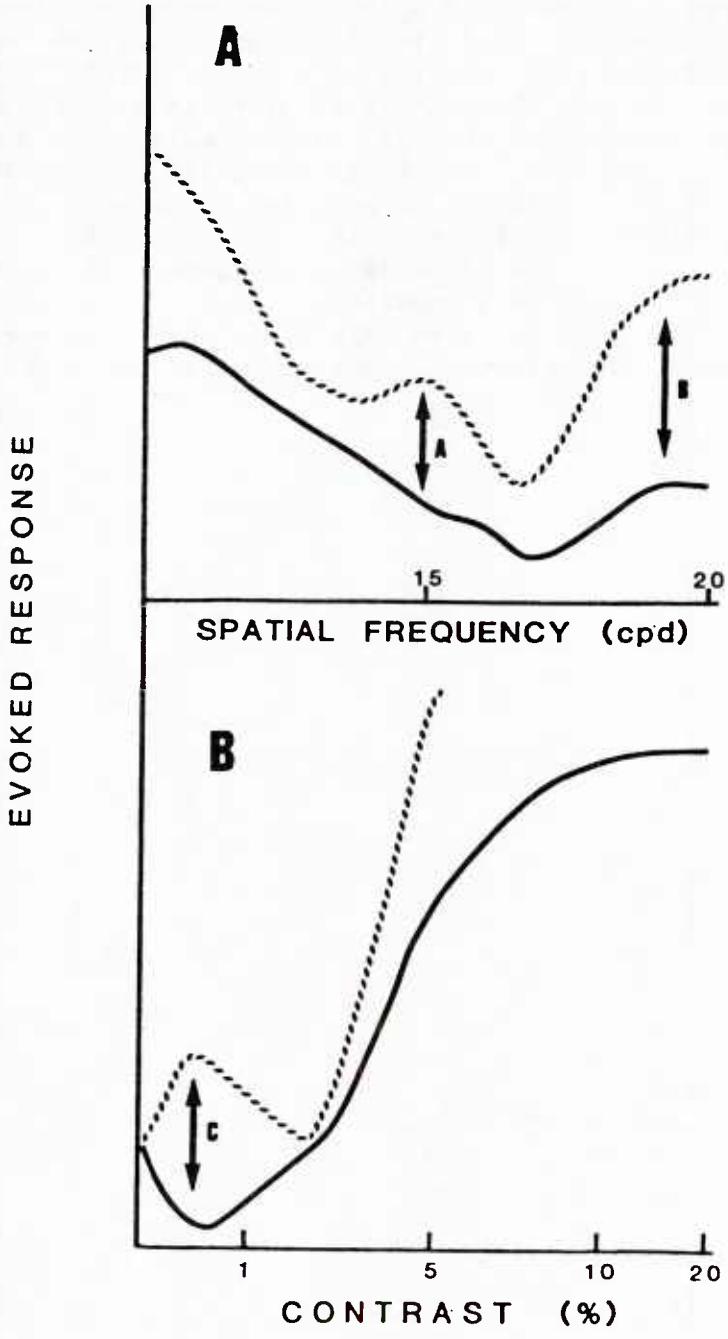


Fig. 16. Phase sensitive detection (PSD, lower **solid curves**) has greater noise immunity than phase-insensitive vector retrieval (**broken curves**). **A, TOP:** Noise pulse during run (**arrow at A**) and rise after threshold (arrow at **B**). 75% contrast sine wave grating modulated at 7 rev/sec and swept in spatial frequency towards the acuity limit. **B, BOTTOM.** PSD retrieval can have good immunity to noise pulse marring indication of threshold (arrow at **C**). 1 cycle/deg sine wave grating modulated at 3 rev/sec and swept in contrast.

In Fig. 16, dashed curves were retrieved with phase-INsensitive (noise prone) vector computation techniques, while the lower solid curves were obtained with an optimally adjusted phase-sensitive detector (**PSD**). The "rise after threshold" pattern we have observed is illustrated at arrow "B" in Fig. 16A; the PSD signal is more immune to this rise, as well as to noise pulses occurring during a run (arrow "A"), which can obfuscate the apparent threshold (arrow "C", Fig. 16B). Beginning an up-sweep run only when the noise level is stable or falling minimizes this latter problem. In conclusion, the activity causing the rise often lacks the same phase as the response, as expected if it originates in a separate, non-visually driven, generator. The way in which EEG noise achieves sufficient phase coherence to pass through the phase-sensitive detector, appearing often as a brief pulse, is considered next.

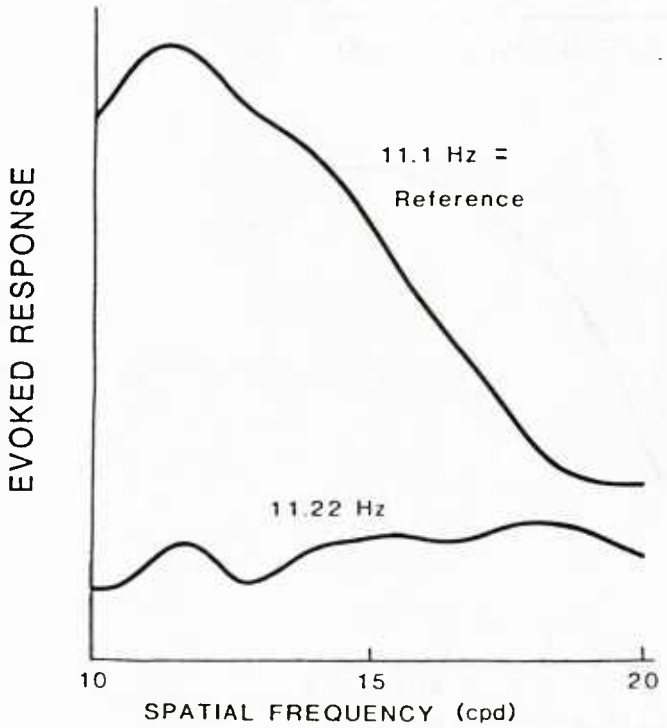


Fig. 17. Lock-ins achieve signal retrieval through frequency selectivity. Upper curve: response to high contrast sine wave grating modulated at 11.1 reversals/sec as spatial frequency is swept to the acuity limit. Lower curve: no response can be retrieved in another lock-in simultaneously set to 11.22 Hz. Time constant, 3 seconds; equivalent noise bandwidth, 0.04 Hz.

The rise after threshold effect implies that visually evoked responses and EEG activity are to some extent mutually exclusive. In our experience and that of others (C. W. Tyler, personal communication) a subject observing a stimulus as it fades to invisibility reaches extremely low levels of scalp activity. Once the stimulus recedes below threshold and "visual attention" presumably relaxes, or if the subject is presented with a blank screen and told to relax prior to a run, the activity is generally higher.

A frequency-selective instrument sees coherent noise. How can we speak of the relative phases of two signals (evoked response and EEG interference) if they differ in frequency? The paradox is resolved upon considering the narrowness of the frequency band of interest. Fig. 17 shows complete attenuation of response at a frequency difference of 0.12 Hz. If noise does get through, we must be dealing with frequency difference even smaller than this. Assume that noise amplitude will be passed if the frequency difference is only 0.05 Hz. At such a small frequency displacement, relative phases will slide past one another very slowly. A 90 deg phase change will take 5 seconds to occur. This phase range (45 deg to either side of a reference signal) is the largest tolerable without much amplitude attenuation. Since cos 45 deg = 0.707, 70% of full amplitude will be passed. Turning to the time period, 5 seconds is long enough to let about 80% of the interference through when the time constant is 3 secs. Thus, non-visually driven generators at the edge of the frequency pass band will produce a noise pulse as they roll past in phase, while generators lying even closer in frequency could hold output at arbitrary positive values (or negative values when phase slides to around 180 from optimal). This is the basis for the DC offsets in baseline, which must be taken into account when extrapolating responses for inferred thresholds (see below). Noise pulses (Fig. 16) imply that EEG interference is not uniformly distributed in frequency across even the narrow 0.04 Hz equivalent noise bandwidth window we employ; rather, the noise can lie at the edge of the band and can therefore "roll by" in phase. In this case, what limited phase coherence we observe with respect to the laboratory reference is an artifact of the instrumentation's frequency selectivity.

The longer-lasting DC offsets imply that EEG interference can at other times maintain phase coherence for much longer than 5 seconds. In these instances, the EEG exhibits innate spectral purity at a frequency we would prefer to have for ourselves.

The baseline: extrapolation to what?

Thresholds are defined by extrapolation to a baseline using the response slope. Previous workers have differed in their choice of baseline, specifying either an absolute zero voltage or an average noise level (Regan, 1975; Tyler, Apkarian & Nakayama, 1978). We have found that neither of these are correct in a biological recording situation. During periods of spontaneous EEG activity the output of the phase-sensitive detector may be actively driven positively or negatively. The instrument is an extremely narrow band device. The frequency stability and phase coherence of that "slice" of the EEG which it sees is sufficiently great to move the post-PSD integrator (capacitor) to positive (or negative) voltage levels for several seconds (see coherent noise section above). The visually evoked response is added to a widely displaced starting level. Only if the output level at the beginning of the response is used as a baseline will extrapolation of the

response slope yield identical threshold estimates. This is illustrated in Fig. 18. Here, the sweeps were begun at two different starting voltages. It can clearly be seen that the response begins its climb at the same contrast value regardless of the initial charge level on the capacitor. The time at which a visually driven response begins as stimulation sweeps upward in intensity will not be related to the absolute zero voltage.

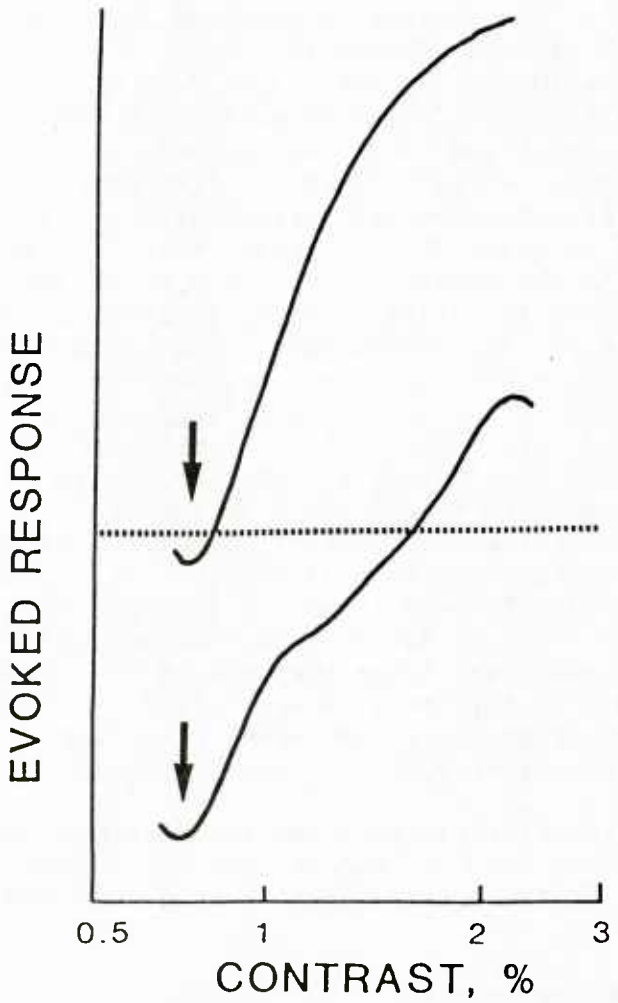


Fig. 18. Due to background EEG activity, the integrator may be at any of a wide range of positive or negative values with respect to electrical zero (dashed line) at the time a run is begun. Correct thresholds (**arrows**) can not be obtained by extrapolation to electrical zero. Instead, the level of the integrator at the time the response begins, termed the turnaround point, must be taken as the baseline. This is the true zero response level.

Assuming an upward sweep, we suggest the following procedure. First, wait for the ongoing activity to drive the output of the phase-sensitive detector channel of interest to a low voltage, thus maximizing the dynamic

range available for response. Secondly, begin a trial when the phase-sensitive detector output is stable or falling slightly in amplitude. This may be achieved by electronically discharging the capacitor or waiting for an opportune time in the ongoing EEG. Under these conditions a well defined starting or turn around point will occur where the response commences, identifying both the starting time and starting voltage level.

This analysis applies only to threshold determination with the swept evoked potential. The output from such experiments are noteworthy in juxtaposing two very different activities: a visually-driven response, and the spontaneous EEG. EEG activity may leave the brain and the retrieval instrument in an unpredictable condition prior to the commencement of a visual response. The dilemma of separating the two activities is less severe with runs of the sort used Tyler et al. (1979), where the stimulus is above threshold for the duration of the data collection period, and the activity is always visually driven.

PART V.
RECENT FINDINGS:
ORIENTATION AND SPATIAL FREQUENCY SELECTIVE LOSSES
in
MULTIPLE SCLEROSIS

Introduction

Multiple sclerosis (**MS**) is a degenerative disease of unknown origin which attacks the myelin sheath of nerve axons. It is thus most commonly regarded as a disease of neural white matter. Symptoms of spinal involvement are common (leg weakness, urinary incontinence). More recently, psychophysical studies (Regan, Silver & Murray, 1977; Regan, Whitlock, Murray & Beverley, 1980) have shown that MS can produce highly selective losses in visual function. For example, contrast sensitivity may be lost for striped (grating) patterns which are vertical, while performance at all other orientations is normal. The first level in the ascending visual system from eye to brain at which orientation selective neurons are found is the visual cortex. The psychophysical findings imply that neurons sharing the same functional role (i.e., showing a common orientation tuning) are affected by the disease while other outwardly similar neurons are not. Such cell bodies lie, by definition, in the cortical grey matter. Their finely myelinated axons may be the locus of attack, but these axons are intracortical fibers, not major nerve fiber bundles like the spinal cord.

The visual performance losses are of interest from the point of view of basic visual science as well as in terms of changing concepts of the disease. The novel effect of interest is a simple loss in contrast sensitivity. However, a wide variety of contour orientations and spatial frequencies must be tested to uncover this hidden deficit, and each eye must be tested separately. The new visual scan (**VSCAN**) technique is well suited

to performing the many tests required, and it performs them quickly and objectively. Furthermore, the ability to document contrast sensitivity losses directly in the visually evoked scalp potential would provide evidence for involvement of the disease in the early sensory coding apparatus of the visual cortex, and help to rule out an interpretation in terms of higher perceptual or cognitive function. Previous visual evoked response (**VER**) testing in MS has shown that the latency prolongation accompanying demyelination can be confined to responses evoked by one stimulus orientation (Camisa, Mylin & Bodis-Wollner, 1981; Coupland & Kirkham, 1982). Latency measures, however, do not permit comparisons between VER and psychophysical results.

Using realtime lock-in retrieval of the visual evoked potential, contrast sensitivity was measured in 15 cases with probable or definite multiple sclerosis and acuities of 20/40 or better. Sine wave grating contrast threshold determinations for three spatial frequencies (1, 4 and 8 cycles/deg) and four orientations (0, 45, 90 and 135 deg) revealed contrast deficits in at least one spatial frequency and orientation in every case. In most cases the visual losses were spotty or multifocal, and not the same in both eyes. Some cases with highly selective patterns of orientation or spatial frequency losses were observed. These are discussed below in terms of cortical involvement in the disease. Since the functional architecture of the visual cortex described in cats and monkeys (i.e., independent columnar systems) may play a role in generating or shaping these losses, we were particularly interested in whether orientation losses could be demonstrated in humans, and whether the ocular dominance, orientation selectivity and spatial frequency selectivity of the losses were linked or independent.

Methods

Stimuli. Sine wave gratings generated by a pattern generator were displayed on a Conrac Model QQA 14N/A video monitor at a mean luminance of 50 cd/m^2 (Photo Research Spectra Spot Meter PR-1500). Background room luminance was approximately 2 cd/m^2. The monitor uses a TV raster with 60 Hz interlaced frames and the reversal rate was asynchronous with respect to this frame rate. The display subtended 8.25 x 11.5 deg of visual angle at the viewing distance of 145 cm. We used a relatively short viewing distance (large stimulus display) to maximize the VEP response.

Contrast $((L_{max} - L_{min})/(L_{max} + L_{min}))$ was varied on a given trial by applying an external control voltage to the pattern generator. Spatial frequency was set at either 1, 4, or 8 cycles/deg. The counterphase flicker modulation frequency was 3.5 Hz (7 reversals/sec), producing cortical potentials at 7 Hz.

Responses. Cortical responses were recorded using a gold cup electrode placed 2.5 cm above the inion and referenced to an ear, using the contralateral ear as ground. The EEG was amplified with a Grass Model P511J pre-amplifier (gain = 10^4). This amplified signal was then shared by a pair of lock-in amplifiers (EG&G/PAR Ortec/Brookdeal 9505/SC; 3 sec time constant). These quadrature instruments furnish four phase detector outputs which, with inversion, are logically equivalent to eight channels, providing retrieval at 45 deg intervals around the clock of all possible

reference phases. A lock-in amplifier achieves signal retrieval from noise through frequency selectivity. This selectivity arises in the phase sensitive detector (**PSD**) stage of the lock-in; the need to adjust optimum phase may be avoided by use of vector retrieval techniques, but these are not noise-immune enough. Therefore our long standing practice is to retrieve responses simultaneously at 4 physical (8 logical) phases. Under these circumstances, the optimal adjustment can never be more than 22.5 deg away from an available channel. The particular phase to be chosen was based upon a vector phase calculation executed one of the quadrature instruments. The output of the lock-ins was stored in a Nicolet 1170 signal averager and plotted for analysis.

Experimental paradigm. Contrast thresholds were estimated by sweeping the contrast of a grating of constant spatial frequency (1,4,8 cycles/deg) and a single orientation (either vertical 0 deg, horizontal 90 deg, 135 deg, or 225 deg). Stimulus spatial frequency was always tested in the order of 1, 8 and 4 cycles/deg, whereas orientation was randomized between trials to lessen adaptation effects. Contrast increased logarithmically from 0.1% to 20% over a 20 sec trial period. A logarithmic stimulus sweep was chosen to improve resolution in the low contrast threshold region, and to aid extrapolation to threshold by linearization of the observed stimulus-response function. During the sweep, subjects were instructed only to fixate a central point; no subjective responses were required. In most cases there was time to repeat spatiotemporal conditions manifesting abnormal sensitivity; these thresholds were replicated.

Patients. Fifteen cases with probable (3) or definite (12) multiple sclerosis (McAlpine, Lumsden & Acheson, 1965) were studied after obtaining informed human consent. All 11 females and 4 males (average age, 31 years) had less than 0.75 diopters astigmatic refractive error. Four cases had nystagmus on eccentric gaze, none in primary gaze, and none had torsional extraocular eye muscle dysfunction. Five cases had a single eye with a history of retrobulbar neuritis, four with residual poor acuity. The 26 remaining eyes had Snellen acuities 20/40 or better, 19 with 20/20 (12 cases). Except for the four eyes above with residual poor acuity, no eye had visual field defects to a 1 or 2 mm white test object (tangent screen at 1m). Optic disc pallor was noted in the eyes with optic neuritis (cases 2, 7, 14 OD; 6, 11 OS) and six additional eyes (cases 4, 15 OU; 11 OD; 14 OS).

Three males and three females with a mean age of 33 years, vision correctable to 20/20 or better, and no history of ophthalmological or neurological disease served as controls for establishing the confidence intervals used in this study. Three were experienced psychophysical observers acquainted with the purpose of the experiment. We noted within a group of 3 experienced and 7 naive observers tested subsequently that there was no statistically significant difference between thresholds for experienced and naive subjects.

Results

Control contrast thresholds showed no statistically significant difference as a function of orientation at any spatial frequency (ANOVA, f=3.5, df 3,32) because the reversal rate selected virtually abolished any oblique effect (see Section III). There was also no statistically significant intraocular difference in thresholds for control subjects within any one spatial frequency (1 cycle/deg t=0.16, df 22; 4 cycles/deg t=0.02, df 20; 8 cycles/deg t=0.11, df 20). Contrast threshold varied with spatial frequency in accord with the normal contrast sensitivity function (visual modulation transfer function; see Section II). Therefore, data for all orientations and eyes for each spatial frequency were combined, and a 99% confidence interval was calculated for normals. These contrasts were as follows: 1 cycle/deg, mean=0.91%, upper 99% confidence interval (CI)=1.85%; 4 cycles/deg, mean=1.14%, upper CI=2.85%; 8 cycles/deg, mean=2.18%, upper CI=5.79%. Only those patient data showing thresholds elevated above the upper 99% CI were considered abnormal.

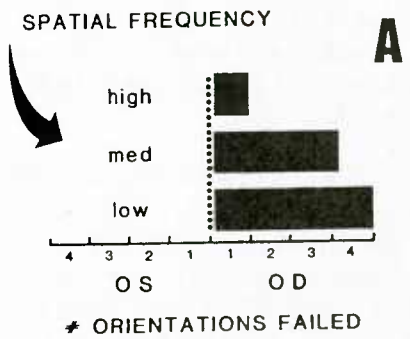


Fig. 19A. Key to Fig. 19B; hypothetical data. Testing results at three spatial frequencies (1, 4, & 8 cycles-/deg) are shown in three separate horizontal bar graphs. The length of the bar graph indicates how many of four separate stimulus orientations elicited abnormally high contrast thresholds. Here, visual loss is strictly unilateral, being confined to the right eye, and is weighted toward lower spatial frequencies.

The scattered, multifocal nature of visual loss is shown for all subjects in Fig. 19. The key to this schematization is given in Fig. 19A. Left and right eyes are shown by bars to the left and right, respectively; 1, 4, and 8 cycles/deg by low, middle and high bars; and number of orientations failed by bar length. Which orientations showed elevated contrast thresholds (failed tests) is illustrated and discussed in detail below for selected subjects. These bar graphs showing number of tests failed (out of 2 eyes x 3 spatial frequencies x 4 orientations) reveal a spotty pattern of loss. Loss may be confined to one eye (bars only leftward, case 12), or may affect only one spatial frequency band or spare only one spatial frequency (case 13, case 9) or loss may be confined to only one orientation (short bars: many cases).

Diagnostic yield was high. All fifteen cases had at least one eye with an elevated contrast threshold at one spatial frequency and orientation (Fig. 19). Eleven of the twelve cases with data from both eyes had some contrast losses in both eyes. The ratio of the elevated contrast thresholds to the control mean averaged 3.6 (SD=1.26, range 1.6 - 7.8) regardless of orientation or spatial frequency. Abnormal contrast sensitivity was spotty

with respect to stimulus orientation, spatial frequency and viewing eye. Multiple orientations were affected in 14 cases (22 eyes). Only one case had contrast losses restricted to a single orientation. Discrete spatial frequency losses occurred less frequently than discrete orientation losses. More than one spatial frequency was involved in 15 eyes of 11 cases. Contrast abnormalities at 1 cycle/deg occurred twice as frequently as those at 4 or 8 cycles/deg. Only two cases (#11 and #13) demonstrated abnormalities at 4 or 8 cycles/deg and not at 1 cycle/deg.

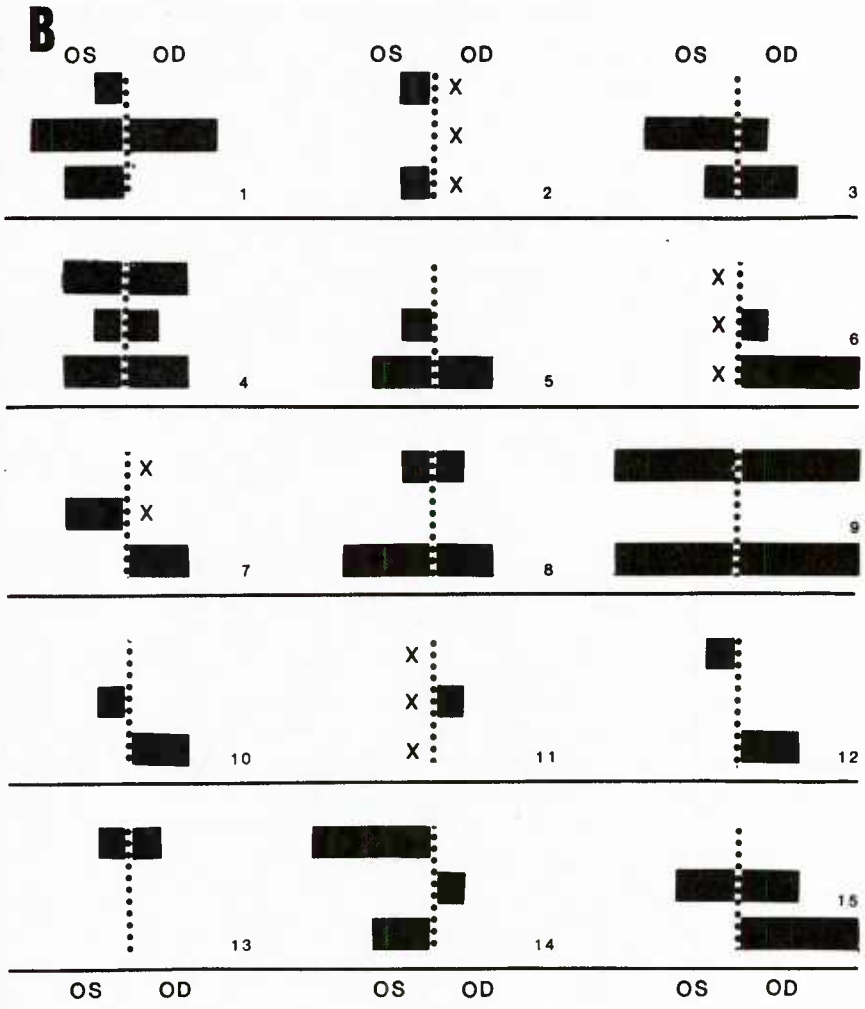


Fig. 19B. Bar graphs showing number of orientations failed per subject for left and right eyes at three spatial frequencies. **OS:** left eye; **OD:** right eye. **X:** not tested. Small numbers are patient codes; results for cases 1, 4, and 9 are shown in greater detail in subsequent Figures.

An example of variability in contrast sensitivity elevations between eyes is shown in Fig. 20 (case #1). At a low spatial frequency (1 cycle/deg), the right eye had uniformly normal contrast thresholds for all orientations, whereas the left eye had elevated thresholds for the vertical and right oblique orientations. The intermediate spatial frequency thresholds were abnormal at all orientations in the left eye. The right eye was also abnormal except for the left oblique which was in the high normal range. At the highest spatial frequency tested, contrast sensitivities were normal in both eyes, except for the vertical in the left eye. Thus, the affected eye can change with change in spatial frequency; at a given spatial frequency, the loss can be confined to one eye at one orientation. Most cases demonstrated interocular variability similar to the above case. In addition, when we compared the interocular differences in absolute contrast thresholds analogously to the interocular comparison of latency (see Discussion), only one patient (case 10) demonstrated an abnormal interocular difference when absolute thresholds for each eye were within the normal monocular range.

Orientation-specific losses which were the same in both eyes were found in 8 cases. In this group as a whole, the losses were not restricted to one orientation or spatial frequency. Case 4 (Fig. 21) illustrates this high degree of similarity in orientation-specific loss between eyes. Contrast thresholds were abnormal (about 35% less sensitive than controls) or at the upper limit of the normal range to the vertical grating at all three spatial frequencies. The right oblique was on the average 5.2 times less sensitive than controls in both eyes at 1 and 8 cycles/deg.

NEXT PAGE:

Fig. 20. Four stripe orientations were tested (symbols at top). Actual contrast thresholds obtained at all 12 spatio-temporal combinations are shown for each eye separately for case 1. Upper, middle and lower pairs of curves shown results with high, medium and low spatial frequencies, given in cycles per degree, **cpd. Circles**, right eye; **Squares**, left eye. **Cross-hatched** region extends from the mean contrast threshold (**arrows**) to the 99% confidence limit for normal observers (means: 0.91% at 1 cycle/deg, 1.14% at 4 cycles/deg and 2.18% at 8 cycles/deg). This patient does not have normal sensitivity, especially at the middle spatial frequency (4 cycles/deg). Losses are variable with regard to both eye and orientation as spatial frequency changes.

PAGE AFTER NEXT:

Fig. 21. Contrast thresholds for Case 4, key as in Fig. 20. Losses are similar in the two eyes, but highly selective for orientation.

Figure 20 this page: (mixed loss)

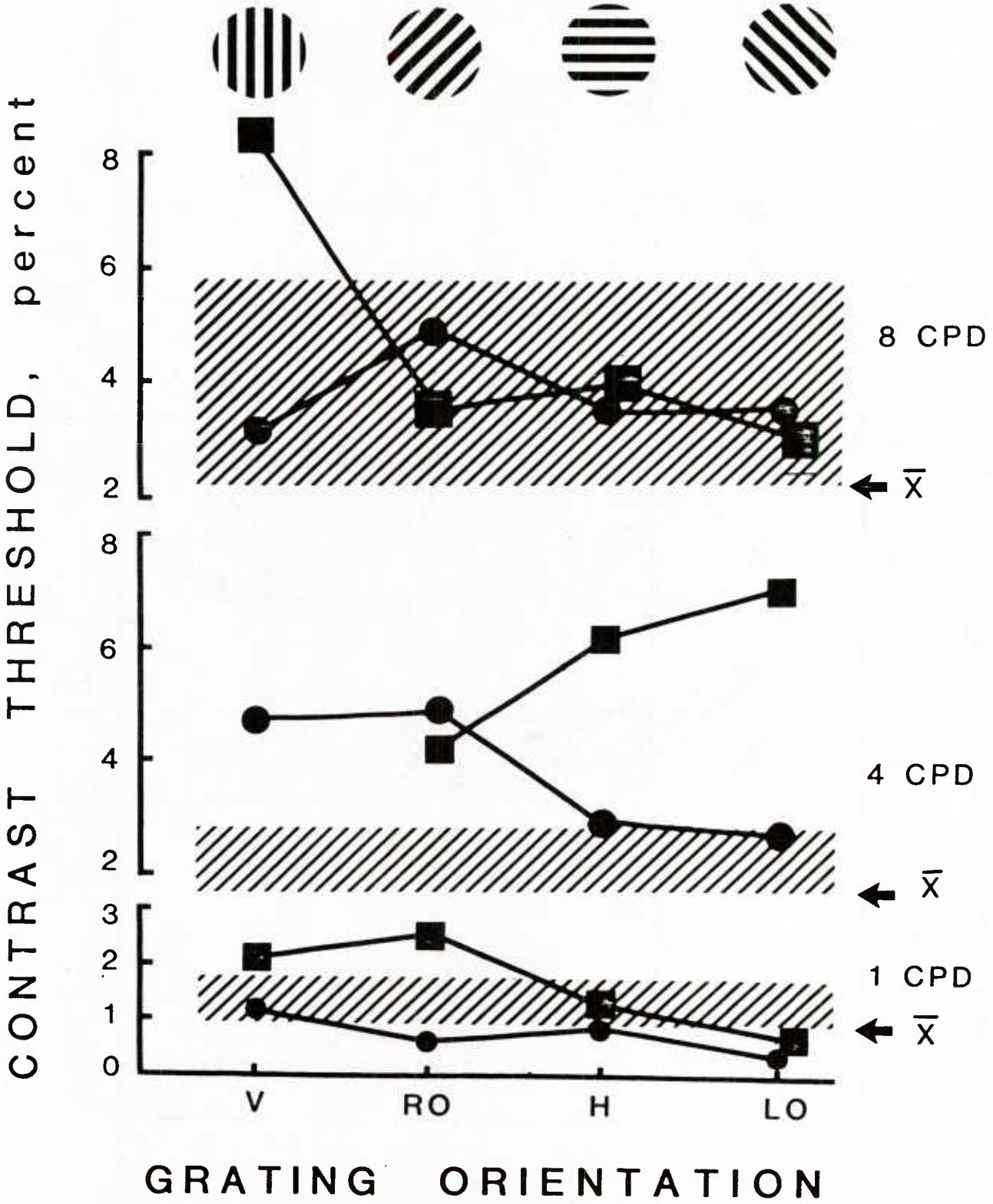
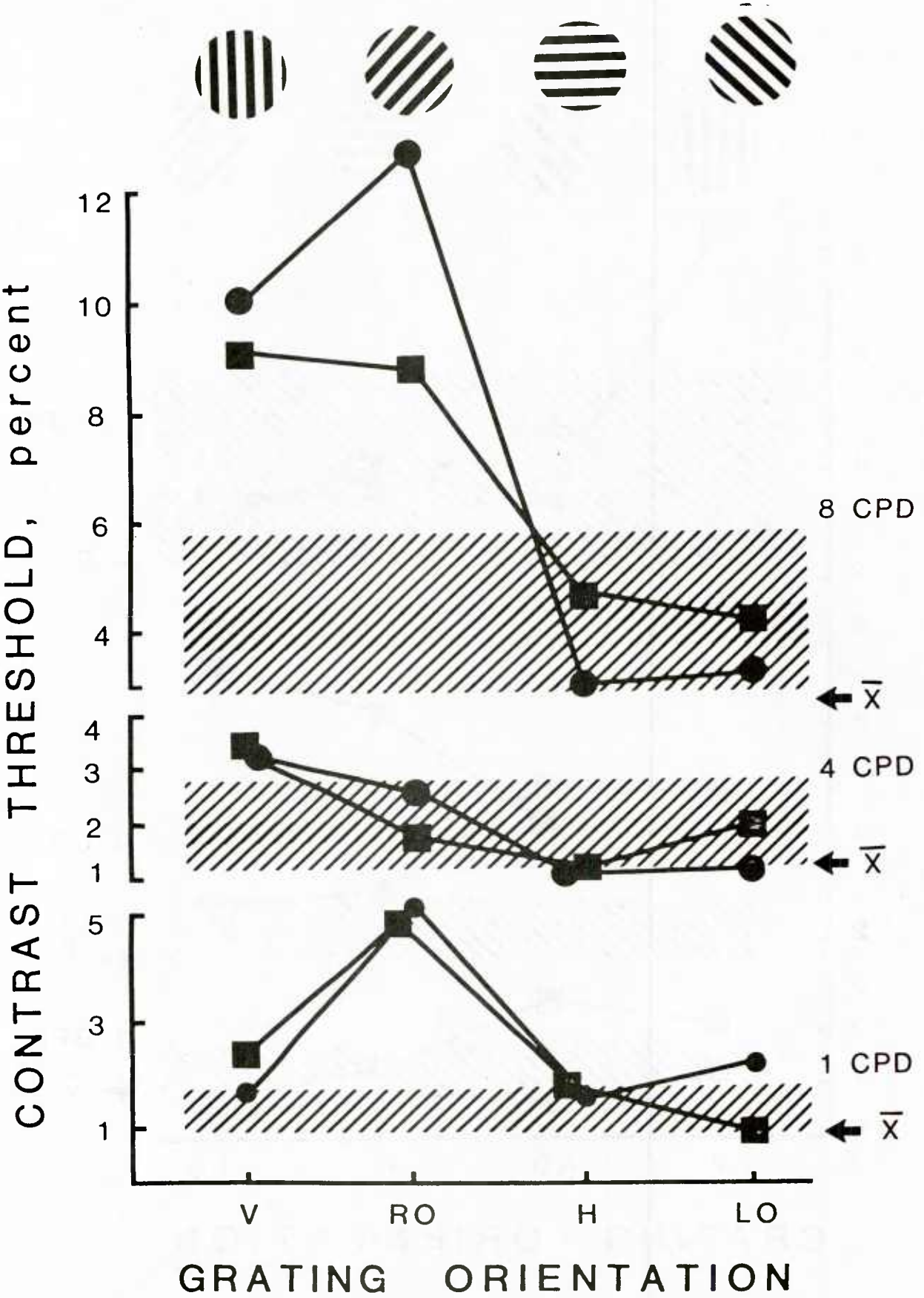


Figure 21 this page: (orientation-specific loss)



Contrast sensitivity abnormalities which were spatial frequency specific were observed infrequently. An example of spatial frequency selectivity is shown in Fig. 22 (case #9). This case was also the sole patient with similar spatial frequency selectivity of contrast sensitivity loss for the two eyes. The right eye was approximately 4.7 times less sensitive than the controls at 1 cycle/deg. At 8 cycles/deg the right and left eyes were on the average 3.9 times less sensitive than the controls. Elevation in contrast thresholds were found at both 1 and 8 cycles/deg, but not at 4 cycles/deg; all orientations are affected.

Discussion

Contrast sensitivity can be reliably measured in a clinical setting with the swept VER. The test is rapid enough to permit testing of several orientation and spatial frequency values in each eye separately.

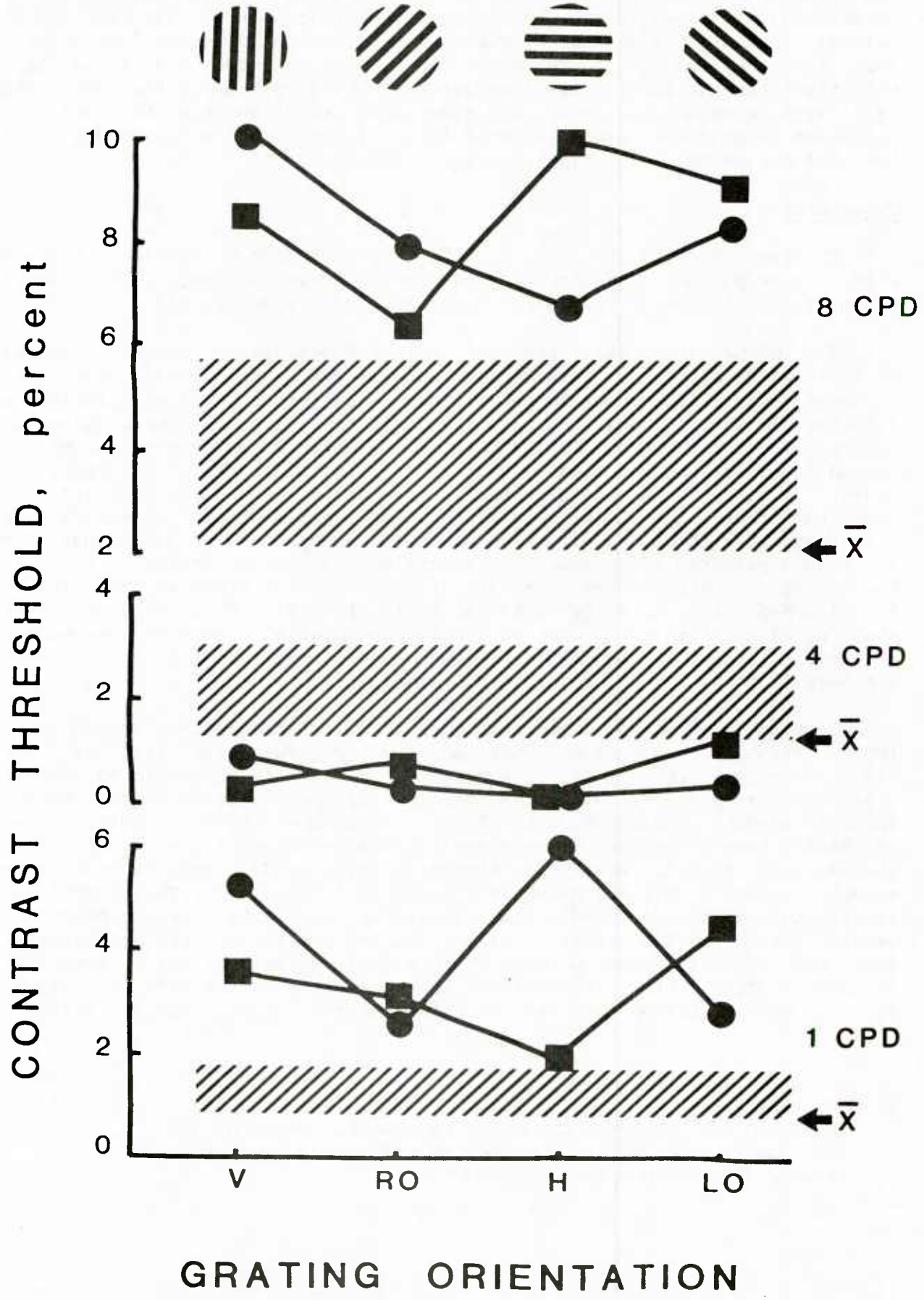
The MS patients tested commonly exhibited orientation-specific losses of contrast sensitivity. These losses were as often uniocular as binocular. Discrete spatial frequency losses occurred less frequently than orientation selective losses. These findings provide an objective electrophysiological confirmation of psychophysically determined orientation-specific contrast threshold elevations reported by Regan, et al. (1980). As in this previous study, no single orientation or spatial frequency seems to be more affected than any other; loses were weighted towards lower spatial frequencies, as only subjects with good acuity were studied. Despite this weighting, the individual patterns of loss was not determined by Snellen acuity. Thus, a number of patients with 20/20 acuity display contrast sensitivity losses at 8 cycles/deg (cases 1, 2, 8, 9, 12 and 13 in Fig. 19). Field defects, which could provide a simple explanation for the low spatial frequency losses, did not exist except in the single case with optic neuritis and poor acuity recovery in whom we could record a VER (case 7).

Cortical involvement. The existence of orientation-selective contrast losses strongly suggests cortical involvement. The first level in the visual pathway where orientation tuning is sufficiently selective to produce these results is the visual cortex, particularly one synapses or more beyond layer IV neurons (Hubel & Wiesel, 1968; Bauer, Dow & Vautin, 1980). Hubel and Wiesel have demonstrated neurophysiologically (Hubel & Wiesel, 1974) and anatomically (Hubel, Wiesel & Stryker, 1977, 1978) that orientation-selective neurons are organized in columns in the cortex. This functional architecture could add orientation selectivity to an otherwise non-selective patchy lesion in the visual cortex. The lesions in MS are classically described at the border between white and grey matter; less commonly, lesions in grey matter not involving adjacent white matter have been noted. Both types of lesion have been described in the visual cortex (Peters, 1958).

NEXT PAGE:

Fig. 22. Contrast thresholds for case 9, key as in Fig. 20. Losses are spatial frequency selective; 4 cycles/deg is spared. Such patterns were not common.

Figure 22 this page: (spatial-frequency selective loss)



In recent anatomical research, intralaminar cortical fibers known classically (von Bonin, 1950) have been shown to include intrinsic axons extending 4 mm in monkey Gilbert & Wiesel, 1983). These axons travel in directions related to the stimulus orientation preference of the neuron from which they arise, and give rise to periodic clustered axonal arborizations thought to be related to periodic columnar architecture. At least along their initial segments, the myelination of these identified fibers is evident with light microscopy (Gilbert, personal communication). Previous electron microscope work has demonstrated myelinated axons throughout the neuropil in cortex (Peters, Palay & Webster, 1976). This is a possible locus of MS attack.

Selective loss and functional architecture. The spatial frequency domain may enjoy cortical columnar organization similar to that of the orientation domain (Silverman, Tootell & De Valois, 1981), with myelin concentrated at areas of spatial frequency selectivity (and orientation non-selectivity; Tootell, Silverman, De Valois & Jacobs, 1983). Evidence has been presented that orientation and spatial frequency selectivity substrates are independent (Berardi, Bisti, Cattaneo, Fiorentini & Maffei, 1982), so that a selective attack on a columnar system for spatial frequency would involve all orientations. Such a result is seen in Case 9 (Fig. 22), where no evidence of optic nerve disease was clinically apparent. Ocular dominance and orientation column systems are also independent (Hubel & Wiesel, 1974). A preferential attack on the orientation column system would be carried across ocular dominance columns, and orientation selective losses would therefore be binocular. Such a result is seen in Case 4 (Fig. 21).

Other possibilities. Although orientation selectivity is not found in the visual pathway prior to the cortex, there is some orientation bias in retinal ganglion cells (cat: Levick & Thibos, 1980; monkey: DeMonasterio, 1978). The bias is weak. In cat, when the stimulus orientation was 90 degrees from the optimal response, the cells still showed some response. This is quite unlike cortical neurons which are narrowly tuned to a specific orientation. The selectivity and severity of the orientation selective contrast losses observed in MS seem too great to be explained by retinal pathology alone.

The elevation in contrast thresholds we observed can not be interpreted as pathological exaggeration of normal orientation anisotropies. Diminished contrast sensitivity for oblique orientations versus horizontally or vertically presented stimuli, (i.e., the oblique effect) can in fact be demonstrated with this technique, but these thresholds are elevated only by a factor 2.5 to 4.3, even under optimal spatial and temporal conditions for obtaining the effect (see Section III). The measured contrast losses in these MS patients were almost always of considerably greater magnitude than an oblique effect and were random with respect to the stimulus orientation among the patients. Additionally, they occurred at spatial frequencies (1 cycle/deg) and at a temporal frequency (7 reversals/sec) where no effect and only a marginal effect respectively can be detected in normal observers with these methods (Section III).

Another cause of orientation specific contrast elevations could be meridional amblyopia. In this instance the losses are greatest at the orientation parallel to the principal meridians of the astigmatism, even when corrected (Mitchell & Wilkinson, 1974). These elevations are seen

particularly at the high spatial frequencies with little effect found at low spatial frequency. Our patients had astigmatic errors less than one diopter; their contrast threshold elevations occurred even at 1 cycle/deg and did not follow the measured astigmatic axis.

Swept technique advantages

Several advantages of the swept stimulus real-time retrieval technique emerge in clinical practice. The major advantage is speed. With speed, more parameters may be tested in a single session. Fatigue and cortical adaptation are minimized. Given the present knowledge of visual neurophysiology, one may chose stimuli for which individual populations of neurons are selective. This makes the "probe" more incisive and the inferred thresholds more amenable to psychophysical and neurophysiological interpretation. The VER can then reliably and objectively assess visual performance rather than only measure latency or waveform changes in disease. In multiple sclerosis, the technique provides a useful indication of subclinical involvement of the visual cortex.

CONCLUSION

The visual evoked potential becomes a powerful tool for basic and clinically applied research when (1) electronically programmed stimulation is combined with (2) real time response retrieval. The possible separation of X and Y streams in the visual system of man would bring a surprising degree of specificity to the messy scalp potential if substantiated. This hypothesis should be pursued with latency, color and central/peripheral visual field balance studies. In clinical research, selective losses in multiple sclerosis are more easily and objectively documented with this method than any other. Such findings will lead to a changed concept of the disease. The findings in multiple sclerosis should be pursued using electronically programmed sweeps of stimulus orientation. This new capability would more rapidly and accurately isolate cases with selective cortical involvement.

I thank my colleagues Mark Kupersmith, MD and W.H. Seiple, Ph.D. for their efforts with a difficult technology. We acknowledge our debt to the pioneering efforts of D. Martin Regan, who long ago urged the widespread application of swept evoked potential methods.

REFERENCES

Adachi, E. & Chiba, J. (1979). Orientation effects on spatial frequency characteristics in human VECPs.
Acta Soc. Ophthalmol. Jap. 83: 2099-2103.

Albus K. (1975). A quantitative study of the projection area of the central and the paracentral visual field in area 17 of the cat. II. The spatial organization of the orientation domain.
Exp. Brain Res. 24: 181-202.

Arden, G.B. (1978). The importance of measuring contrast sensitivity in cases of visual disturbance.
Br. J. Ophthal. 62: 198-209.

Arundale, K. (1978). An investigation into the variation of human contrast sensitivity with age and ocular pathology.
Br. Jl Ophthal. 62: 213.

Aunon, J.I., McGillem, C.D. & Childers, D.G. (1981). Signal processing in evoked potential research: averaging and modeling.
In J. R. Bourne, Ed., **Critical Reviews in Bioengineering.**
Boca Raton, FL: CRC, 323-367.

Bauer, R, Dow, BM, and Vautin, RG (1980). Laminar distribution of preferred orientations in foveal striate cortex of the monkey.
Exp. Brain Res. 41: 54-60.

Bauer, J.A., Owens, D.A. Thomas, J. & Held, R. (1979). Monkeys show an oblique effect.
Perception 8: 247-253.

Berardi, N, Bisti, S, Cattaneo, A, Fiorentini, A, and Maffei, L (1982). Correlation between the preferred orientation and spatial frequency of neurons in visual areas 17 and 18 of the cat.
J. Physiol. 323: 603-618.

Berkley, M.A., Kitterle, F. & Watkins, D.W. (1975). Grating visibility as a function of orientation and retinal eccentricity.
Vision Res. 15: 238-244.

Bisti, S. & Maffei, L. (1974). Behavioural contrast sensitivity of the cat in various meridians.
J. Physiol. (Lond.) 241: 201-210.

Boltz, R.L., Hanverth, R.S. & Smith, E.L. (1979). Orientation anisotropy of visual stimuli in rhesus monkeys: a behavioral study.
Science 205: 511-513.

Bonds, A.B. (1982). An oblique effect in the visual evoked-potential of the cat.
Expl Brain Res. 46: 151-154.

Bonin, von G (1950). Essay on the cerebral cortex. Springfield, IL: Thomas.

Bostrom, C., Keller, E.L. & Marg, E. (1978). A reconsideration of visual evoked potentials for fast automated ophthalmic refractions. Invest. Ophthal. vis. Sci. 17: 182-185.

Camisa, J.M., Blake, R. & Lema, S. (1977). The effects of temporal modulation on the oblique effect in humans. Perception 6: 165-171.

Camisa, J, Mylin, LH, and Bodis-Wollner, I (1981). The effect of stimulus orientation on the visual evoked potential in multiple sclerosis. Annals Neurology 10: 532-539.

Campbell, F.W. and Green, D.G. (1965). Optical and retinal factors affecting visual resolution. J. Physiol. 181: 576-593.

Campbell, F.W. and Kulikowski, J.J. (1971). An electrophysiological measure of the psychophysical contrast threshold. J. Physiol. 217: 54P.

Campbell, F.W. and Kulikowski, J.J. (1972). The visual evoked potential as a function of contrast of a grating pattern. J. Physiol. 222: 345.

Campbell, F.W. & Maffei, L. (1970). Electrophysiological evidence for the existence of orientation and size detectors in the human visual system. J. Physiol. 207: 635-652.

Coupland, SG and Kirkham, TH (1982). Orientation-specific visual evoked potential deficits in multiple sclerosis. Canad. J. Neurol. 9: 331-337.

Childers, D.G., Doyle, T.C., Brinck, A.G. & Perry, N.W. (1972). Ensemble characteristics of the human visual evoked response: periodic and random stimulation. IEEE Trans. Biomed. Engg. BME-19: 408-415.

De Valois, R.L., Yund, E.W. & Hepler, N. (1982). The orientation and direction selectivity of cells in macaque visual cortex. Vision Res. 22: 531-544.

Enoch, J.M., Shinichi, Y., Namba, A. (1979). Contrast (modulation) functions measured in patients with high refractive error with emphasis on aphakia. I. Theoretical considerations. Documenta Ophthal. 47: 139-145.

Enroth-Cugell, C. & Robson, J.G. (1966). The contrast sensitivity of retinal ganglion cells of the cat. J. Physiol. 187: 517-552.

Gilbert, C.D. (1983). Microcircuitry of the visual cortex. Ann. Rev. Neuroscience 6:217-247.

Gilbert, CD and Wiesel, TN (1983). Clustered intrinsic connections in cat visual cortex.
J. Neuroscience 3: 1116-1133.

Ginsburg, A.P. & Cannon, M.W. (1983). Comparison of three methods for rapid determination of threshold contrast sensitivity.
Invest. Ophthal. vis. Sci. 24: 798-802.

Green, M. (1981). Psychophysical relationships among mechanisms sensitive to pattern, motion and flicker.
Vision Res. 21: 971-983.

Henry, G.H. (1977). Receptive field classes of cells in the striate cortex of the cat.
Brain Res. 133: 1-28.

Hubel, DH and Wiesel, TN (1968). Receptive fields and functional architecture of monkey striate cortex.
J. Physiol. 195: 215-243.

Hubel D.H. & Wiesel, T.N. (1974). Sequence regularity and geometry of orientation columns in the monkey striate cortex.
J. comp. Neurol. 158: 267-293.

Hubel D.H., Wiesel T.N. & Stryker M.P. (1977). Orientation columns in macaque monkey visual cortex demonstrated by the 2-deoxyglucose autoradiographic technique.
Nature 269: 328-330.

Hubel D.H., Wiesel, T.N. & Stryker M.P. (1978). Anatomical demonstration of orientation columns in Macaque monkey.
J. comp. Neurol. 177: 361-380.

Jones, K.R. & Berkley, M.A. (1982). Loss of temporal sensitivity in the dorsal lateral geniculate nucleus and Area 18 of the cat following monocular deprivation.
J. Neurophysiol. (in press).

Kelly, D.H. (1977). Visual contrast sensitivity.
Optica Acta 24: 107.

Kennedy, H. & Orban, G.A. (1979). Preferences for horizontal or vertical orientation in cat visual cortical neurones.
J. Physiol. (Lond.) 296: 61P-62P.

Kulikowski, J.J. (1978). Pattern and movement detection in man and rabbit: separation and comparison of occipital potentials.
Vision Res. 18: 183-189.

Kupersmith, M.J., Nelson, J.I., Seiple, W.H., Weiss, P., and Carr, R. (in press). The 20/20 eye in multiple sclerosis.
Neurology.

Lehmann, D., Beeler, G.W.,Jr., & Fender, D.H. (1965). Changes in patterns of the human electroencephalogram during fluctuations of perception of stabilized retinal images.
Electroen. clin. Neurophysiol. 19: 336-343.

Lehmkuhle, S., Kratz, K.E., Mangel, S.C. & Sherman, S.M. (1980). Spatial and temporal sensitivity of X-cells and Y-cells in dorsal lateral geniculate nucleus of the cat.
J. Neurophysiol. 43: 520-541.

Lennie, P. (1980). Parallel visual pathways: a review.
Vision Res. 20: 561-594.

Leventhal, A.G. & Hirsch, H.V.B. (1977). Effects of early experience upon orientation sensitivity and binocularity of neurons in visual cortex of cats.
Proc. natn. Acad. Sci. U.S.A. 74: 1272-1276.

Levick, WR and Thibos, LN (1980). Orientation bias of cat retinal ganglion cells.
Nature 286: 389-390.

Lund, J.S. & Boothe, R.G. (1975). Interlaminar connections and pyramidal neuron organisation in the visual cortex, Area 17, of the Macaque monkey.
J. comp. Neurol. 159: 305-334.

Maffei, L. & Campbell, F.W. (1970). Neurophysiological localization of the vertical and horizontal visual coordinates in man.
Science, N.Y. 167: 386-387.

Mansfield, R.J.W. (1974). Neural basis of orientation perception in primate vision.
Science, N.Y. 186: 1133-1135.

Mansfield, R.J.W. & Ronner, S.F. (1978). Orientation anisotropy in monkey visual cortex.
Brain Res. 149: 229-234.

McAlpine, D, Lumsden, CE, and Acheson, ED (1965). Multiple Sclerosis. A Reappraisal. Baltimore: Wilkins, 415 pp.

Mitchell, DE and Wilkinson, F (1974). The effects of early astigmatism on the visual resolution of gratings.
J. Physiol. 243: 739-756.

Morrell, L.K. (1966). Some characteristics of stimulus-provoked alpha activity.
Electroen. clin. Neurophysiol. 21: 552-561.

Movshon, J.A., Tolhurst, D.J., and Dean, A.F. (1982). How many neurons are involved in perceptual decisions?
Invest. Ophthal. vis. Sci. 22 (ARVO suppl): 207.

Mulholland, T. & Evans, C.R. (1965). An unexpected artefact in the human electroencephalogram concerning the alpha rhythm and the orientation of the eyes.
Nature (Lond.) 207: 36-37.

Mustari, M.J., Bullier, J. & Henry, G.H. (1982). Comparison of response properties of three types of monosynaptic S-cell in cat striate cortex. J. Neurophysiol. 47: 439-454.

Nakayama, K., Mackeben, M. & Sutter, E. (1980). Narrow spatial and temporal frequency tuning in the alert monkey VEP.
Brain Res. 193: 263-267.

Nelson, J.I. (1974). Motion sensitivity in peripheral vision.
Perception 3: 151-152.

Nelson, J.I., Kupersmith, M.J., Seiple, W.H., and Carr, R.E. The swept display technique: separation of X- and Y-dominated evoked potentials. In R. Nodar & C. Barber, eds., Evoked Potentials II. New York: Butterworths, in press, 1982.

Orban G.A. & Kennedy, H. (1981). The influence of eccentricity on receptive field types and orientation selectivity in Areas 17 and 18 of the cat.
Brain Res. 208: 203-208.

Payne, B.R. & Berman, N. (1983). Functional organization of neurons in cat striate cortex: variations in preferred orientation and orientation selectivity with receptive-field type, ocular dominance, and location in visual-field map.
J. Neurophysiol. 49: 1051-1072.

Peters, G (1958). Multiple sklerose. in W. Schotz (Ed.) Handbuch der patholog ische anatomie und histologie, Zweiter Teil.
NY: Springer-Verlag.

Peters, A, Palay, SL, and Webster, H de F (1976). The Fine Structure of the Nervous System. The Neurons and Supporting Cells.
Philadelphia: Saunders, p. 308-315.

Pettigrew, J.D., Nikara, T., & Bishop, P.O. (1968). Responses to moving slits by single units in cat striate cortex.
Exp. Brain Res. 6: 373-390.

Regan, D. (1966). Some characteristics of average steady-state and transient responses evoked by modulated light.
Electroen. clin. Neurophysiol. 20: 238-248.

Regan, D. (1968). A high frequency mechanism which underlies visual evoked potentials.
Electroen. Neurophysiol. 25: 231-237.

Regan, D. (1973). Rapid objective refraction using evoked brain potentials.
Invest. Ophthal. vis. Sci. 12: 669-679.

Regan, D. (1975). Colour coding of pattern responses in man investigated by evoked potential feedback and direct plot techniques. Vision Res. 15: 175-183.

Regan, D. (1977). Speedy assessment of visual acuity in amblyopia by the evoked potential method. Ophthalmologica 175: 159-164.

Regan, D. (1980). Speedy evoked potential methods for assessing vision in normal and amblyopic eyes: pros and cons. Vision Res. 20: 265-269.

Regan, D. (1981). Evoked potential studies of visual perception. Canad. J. Psychol. 35: 77-112.

Regan, D., Silver, R. and Murray, T.J. (1977). Visual acuity and contrast sensitivity in multiple sclerosis: hidden visual loss. Brain 100: 563-579.

Regan, D., Whitlock, J.A., Murray, T.J. & Beverley, K.I. (1980). Orientation-specific losses of contrast sensitivity in multiple sclerosis. Invest. Ophthal. vis. Sci. 19: 324-328.

Robson, J.G. (1966). Spatial and temporal contrast-sensitivity functions of the visual system. J. opt. Soc. Amer. 56: 1141-1142.

Sekuler, R., Hutman, L.P., and Owsley, C.J. (1980). Human aging and spatial vision. Science 209: 1255-1256.

Sekuler, R.W. & Tynan, P. (1977). Rapid measurement of contrast-sensitivity functions. Am.J. Optom.physiol. Optics 54: 573-575.

Senmoto, S. & Childers, D.G. (1972). Adaptive decomposition of a composite signal of identical unknown wavelets in noise. IEEE Trans. Systems, Man & Cybernetics SMC-2: 59-66.

Sherman, S.M. (1982). Parallel pathways in the cat's geniculocortical system: W-, X-, and Y-cells. In A. R. Morrison & P. L. Strick, eds. Changing Concepts of the Nervous Systems. New York: Academic, 337-359.

Silverman, MS, Tootell, RBH, and De Valois, RL (1981). Electrophysiological verification of deoxyglucose spatial frequency columns in cat striate cortex. Society for Neuroscience Abstracts 11: 356.

Srebro, R., Sokol, B., and Wright, W. (1981). The power spectra of visually evoked potentials in pseudorandom contrast reversals of gratings. EEG Clin. Neurophysiol. 51: 63-68.

Stone, J., Dreher, B. & Leventhal, A. (1979). Hierarchical and parallel mechanisms in the organization of visual cortex. Brain Res. Rev. 1: 345-394.

Tootell, RBH, Silverman, MS, De Valois, RL, and Jacobs, GH (1983). Functional organization of the second cortical visual area in primates. Science 220: 737-739.

Tyler, C.W., Apkarian, P. & Nakayama, K. (1981). High temporal frequency visual evoked potentials to luminance and pattern stimulation in the peripheral retina. In C. Barber, Ed., Evoked Potentials. Proceedings of an International Evoked Potentials Symposium, Nottingham, U.K., p. 199-204. MTP Press.

Tyler, C.W., Apkarian, P.A., Levi, D.M. & Nakayama, K. (1979). Rapid assessment of visual function: an electronic sweep technique for the pattern visual evoked potential.
Invest. Ophthal. vis. Sci. 18: 703-713.

Tyler, C.W., Apkarian, P.A. & Nakayama, K. (1978). Multiple spatial-frequency tuning of electrical responses from human visual cortex.
Expl Brain Res. 33: 535-550.

Tyler, C.W., & Nakayama, K., Apkarian, P.A., & Levi, D.M. (1981). VEP assessment of visual function.
Vision Res. 21: 607-609.

Vandenbussche, E. & Orban, G.A. (1980). Differential orientation thresholds as a function of orientation in the cat.
Archs int. Physiol. Biochem. (Belgium) 88: P11-P12.

Vandenbussche, E. & Orban, G.A. (1981). Effect of orientation on absolute and differential grating acuity thresholds of the cat.
Archs int. Physiol. Biochem. (Belgium) 89: P52-P53.

Zemon, V., Gutowski, W. & Horton, T. (1981). A neurophysiological and psychophysical study of the oblique effect. Presented at Recent Advances in Vision, Topical Meeting of the Optical Society of America, 30 April - 3 May, Sarasota, FL.

--- end refs

DISTRIBUTION LIST

REPORT NO. NADC-84101-60
Contract No. N62269-82-C-0247

	No. of Copies
Director, Defense Technical Information Center	12
Commander, Naval Air Systems Command	10
(4 for NAVAIRDEVCEN Liaison Office)	
(3 for AIR-310C)	
(2 for AIR-340B)	
(1 for AIR-531B)	
Chief of Naval Material	2
(1 for MAT-05)	
Commanding Officer, Naval Medical Research & Development Command	2
(1 for NMRDC-44)	
Chief, Bureau of Medicine & Surgery	2
(1 for NM&S 3C1)	
Chief of Naval Operations	3
(1 for NOP-05H)	
(1 for NOP-098E)	
Chief of Naval Research	5
(1 for ONR-440)	
(1 for ONR-441)	
(1 for ONR-441NP)	
(1 for ONR-442)	
Commander, Naval Safety Center	1
Commanding Officer, Naval Aerospace Medical Research Laboratory	1
Superintendent, Naval Postgraduate School	1
Commanding Officer, Naval Health Research Center	1
Commanding Officer, Naval Personnel Research & Development Center	1
Commander, Naval Air Test Center	1
Commanding Officer, Naval Biodynamics Laboratory	1
Commanding Officer, Naval Submarine Medical Research Laboratory	1
Commanding Officer, Naval Training Equipment Center	1
Directorate of Life Sciences	1
Air Force Aerospace Medical Research Laboratory	1
Crew Technology Division	1
U.S. Army Aeromedical Research Laboratory	1
FAA Civil Aeromedical Institute	1
Biomedical Research Divison	2
Biomedical Laboratories	1
Dr. Lenard Matin, Visual Science Laboratory	1
Dr. Aaron Lewis, School of Applied & Engineering Physics	1
Dr. A. Terrance Bahill, Biomedical Engineering Program	1
Dr. Bruce A. Eisenstein, Head Department Electrical & Computer Engineering and Dr. Banu Onaral	2
Dr. Mike L. Walbarsht, Professor of Opthalmology and Biomedical Engineering	1
Royal Air Force Institute of Aviation Medicine	1
Defense & Civil Institute of Environmental Medicine	1
German Air Force Institute of Aerospace Medicine	1
Institute of Aviation Medicine	1